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THE PATHOLOGY AND TREATMENT OF YELLOW FEVER;

WITH SOME REMARKS UPON

THE NATURE OF ITS CAUSE AND ITS PREVENTION.

BY

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This Work I Dedicate

TO MY DISTINGUISHED PRECEPTOR AND FRIEND,

PROF. JOSEPH LEIDY, M.D.,

OF THE UNIVERSITY OF PENNSYLVANIA,

WHO FIRST TAUGHT ME THE PRINCIPLES OF EXACT SCIENCE,

AND WHOSE SYMPATHY AND KINDNESS

HAVE BEEN TO ME,

IN ALL THE CONJUNCTURES OF LIFE,

A NEVER-FAILING

Solace and Support.

PREFACE

In preparing this Treatise on Yellow Fever, the object I have kept steadily in view, has been to draw as distinct and correct a sketch of its various pathological phenomena, and their mutual relations, as our present knowledge of the disease permits.

Though I indulge the hope that my purpose has been to some extent accomplished, I am not blind to the numerous and important gaps which are left, to be filled, hereafter, by further systematic investigations. But imperfect as the present work must, of necessity, be, I trust it will serve as a guide to the practicing physician in his efforts to master this most malignant disease.

While the observations of the clinical phenomena were chiefly made at the bedside of my private patients during several epidemics, the pathological studies were pursued, for the most part, in the dead-house and pathological laboratory of the Charity Hospital of this city; an institution which, for the study of yellow fever, probably offers more favorable opportunities than any other situated in the yellow fever zone.

Having on several occasions been disappointed by lithographers making inaccurate copies of my original pencil-drawings, I have made the attempt to lithograph the illustrations accompanying this work, upon the stone myself. Though they may not be finished as exquisitely as by the hand of a first-class professional artist, I have, at least, the satisfaction of knowing that they represent the tissues, accurately, as I observed them under the microscope.

New Orleans, La., May, 1880.

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INTRODUCTION.

There are few infectious diseases which have engaged the interest of medical men as much as yellow fever. In consequence, the literature of this disease, beginning in the seventeenth century and extending to our time, has assumed very considerable dimensions.* But extensive as this literature appears, it has, in reality, but little advanced our knowledge of the true pathology of this disease, for the reason that the authors, especially the older ones, had contented themselves with basing their pathological theories chiefly upon the clinical phenomena observed at the bedside, or, at the utmost, upon the macroscopical examinations accompanying the autopsies, which, as may be presumed, were not always made in the systematic style and manner essential to an accurate scientific investigation. Accordingly, the authors principally confined their writings to a description of the history of the disease, or to the observations which they made at the bedside, and from which they formed their various speculative theories as to its probable cause.

From these remarks, however, it must not be inferred that our predecessors were inferior students or observers, for their clinical observations have in most points been corroborated by our own; their deficiency of observation was only due to want of acquaintance with those important pathological facts, elicited chiefly by the aid of the microscope in more recent times; for, twenty-five years have hardly elapsed since this instrument was first used to demonstrate the structural changes taking place in various organs during the course of yellow fever. In judging, therefore, of the merits of our predecessors, the rapid progress made in our own time in human physiology and pathology, upsetting many of the

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* The works and monographs treating upon yellow fever, and composing the Bibliography of Dr. *La Roche's* great work on this disease, *alone*, amount to *nine hundred and seventy-five.*

older theories, must be taken into consideration. Thus, the former theories of the processes of fever and inflammation have been placed upon different bases, greatly by the labors of Virchow. The febrile process was still shrouded in mystery, until, not many years ago, by numerous experiments relating to the interchanges of matter and the production of heat in the blood during this process, more light was thrown upon it. With the knowledge of modern pathology, therefore, the nature of yellow fever should now be more successfully studied, and means be devised to mitigate, at least, the disease, and deprive it of its terror. The systematic and thorough labors of European pathologists into the pathology and treatment of small-pox, typhus and typhoid fever, diphtheria, and other infectious diseases, may serve as an example. The late epidemics at New Orleans and Memphis have furnished sufficient material for such studies; and though we earnestly hope that these calamities will not be witnessed again, we must presume that sporadic cases of yellow fever will always occur to serve for more thorough and systematic studies than have hitherto been made.

The future studies into the pathology of yellow fever, however, in order to be productive, should be made with sufficient accuracy and system, as otherwise they could only give rise to false impressions and confusion. The clinical phenomena of the individual cases, particularly the comparative state of the pulse and temperature, the gastric and nervous phenomena, the apparent condition of the bowels and bladder, and the frequency and character of the discharges from the latter organs should be closely observed and carefully noted, in order to be accurately compared with the pathological changes met with in the various organs after death. It is only from investigation of this kind, systematically pursued with the necessary accuracy of observation by trustworthy and experienced pathologists, who are, besides, thoroughly acquainted with the normal structure of the organs, that additional facts may be elicited. Such labors, however, are not as easily and as readily performed as is imagined. The possession and the knowledge of handling a microscope do not suffice for the correct recognition and determination of pathological changes, nor do they qualify every microscopic operator for labors

as important as these; for, besides the experience essential to an accurate examination, the microscopist should also possess the necessary knowledge and experience in the proper preparation of the tissues, in order to preserve their integrity, or render them otherwise fit for microscopical examination. This knowledge is only possessed by a comparatively small number of those who use the microscope. Besides this, the investigator should possess a free and unbiased judgment, so that he may be able to look upon things as they really are, and examine the subject from different sides and in various manners, before he takes up the pen. Many false statements have been made for the want of the proper qualification for accurate scientific research, and sometimes, I am sorry to say, have been made for the sole object of public notoriety, the common tendency of the day. In such cases, much honest labor is required to remedy the confusion, and to erase the false impressions made upon the medical mind by inconsiderate and erroneous statements.

It must be obvious to every rationally thinking mind, that for the mitigation or prevention of yellow fever, an intimate acquaintance with the pathology of this disease is absolutely necessary, and must form the basis of all inquiries or investigations, made in relation to its cause. It is for the general want of this thorough knowledge that so many speculative theories have arisen, concerning the nature of the cause of this disease. To obtain a more definite idea of the nature of the cause, however, is not the only object of acquiring a correct knowledge of the pathology of the disease, for there is another of more vital moment depending upon it, viz., its *rational treatment.*

Though in the more recent epidemics of yellow fever the treatment pursued by the better educated physicians has been more rational and less empirical than in former times, it cannot be denied that during an epidemic, when the demand for doctors is unusually great, a considerable portion of the medical forces called into requisition for treating and curing the many hundreds of cases, are but very imperfectly prepared for the proper discharge of such a duty; this portion of the medical profession, however, might be better qualified if they were a little more acquainted with the true pathology of the disease, a knowl-

edge upon which they could more safely rely in the selection of their remedies than upon too great confidence in their materia medica. And it is the earnest desire of counteracting the pernicious influence of quackery, prevailing to a considerable extent during each epidemic of yellow fever, and which cannot be but humiliating to the better part of the medical profession, that particularly prompts me to write this treatise. For this reason, no space will be wasted in a description of the history of the disease, or of the various epidemics which have prevailed in the different localities of the globe, for these subjects have been commented on so often as now to be familiar to every physician and layman. On the contrary, I shall confine myself to practical points, which directly bear upon the final mitigation or amelioration of the disease, and take the reader at once to the bedside, where he may study the clinical phenomena. From the sick-room, I shall take him to the dead-house to witness the macroscopical examination of the organs by the autopsy, and thence to the pathological laboratory, to obtain a knowledge of the microscopical pathological changes which, during the course of the disease, have taken place in the various tissues and organs. After being thoroughly acquainted with these facts, we are ready to enter into a comparison of the clinical phenomena with the pathological changes of the organs found after death, and synthetically to build up a general pathology, to be followed by a study of the probable nature of the cause, and the rational treatment of the disease. Lastly, after having thus studied and determined the character of yellow fever, and furthermore considered all points relating to it, we may venture to make a few remarks on its prevention.

PART I.

CLINICAL PHENOMENA OBSERVED DURING THE COURSE OF THE DISEASE.

Most authors state that an attack of yellow fever rarely announces itself by any prodromal symptoms, but, in most cases, rather takes the patient by surprise. There are, nevertheless, many cases in which the fever is preceded by certain initiatory symptoms, similar to those observed in other infectious diseases, and consisting in a general feeling of uneasiness or discomfort, a want of the usual appetite, a certain degree of lassitude, more or less headache, etc., symptoms depending upon a general depression of the nervous system, and due to the action of the specific poison of the disease. In this condition the patient may remain for many days, especially when the disease prevails in the form of an epidemic, and when his mind is troubled with the cares and duties of family or friends, or by the general suffering and misery of which he is a daily witness,—or, he may succumb after the lapse of only a few hours. Nor is there any particular time for the insidious attack to take place. The patient may be surprised in the morning, or during the day, while engaged in business, or in the evening, and even during sleep. Although in most instances the disease appears suddenly, I am inclined to think that this phenomenon is more apparent than real, and, with the exception of very slight ephemeral cases, it is more probable that the fever is generally preceded by some prodromal phenomena, which, slight as they may be, announce its approach, especially in cases of a more severe and typical character. As the physician rarely observes the disease at the moment when the patient is first conscious of it, these forebodings, the prodromes, are usually overlooked—the patient himself not having been aware of them, as his mind was perhaps too much engaged with

other matters. Thus, children are frequently attacked while playing with their toys, unconscious of the enemy who steals upon them and threatens their life; and, in many instances, the parents are not warned of the danger until they perceive the flushed face and heated skin of their child. It is generally accepted that in yellow fever, as in other infectious diseases, there is a period of incubation, which, commencing with the time of the absorption of the poison by the organism, may vary in length from a few hours to a number of days, or even weeks, during which time the poison, by increasing in quantity, is, so to say, getting ready for the attack. We may justly presume that such a period really exists, as there is no positive evidence that the fever ever suddenly appeared immediately after the exposure of the patient to the influence of the noxious poison; and, furthermore, that it appears quite improbable that the same poison should, during this whole period, remain dormant, without giving rise to any external phenomena indicating its presence in the system.

However slight or severe the prodromal phenomena may be, the real attack of the disease commences with the first symptoms of the febrile process. In most cases, perhaps, the disease is ushered in by an alternate sensation of chilliness and heat, associated with dryness of the skin; though many cases commence with a decided rigor. At the same time the patient suffers with pains in the head, back and limbs. The headache, which, to a slight extent, may already have existed as one of the prodromes, is chiefly confined to the forehead and temples—from which localities it may extend in an inferior degree over the rest of the head—and seems to be peculiar in character. The pain I experienced, even during a mere ephemeral attack of yellow fever, which I had, appeared to me more deeply seated than the neuralgic or rheumatic cephalalgia, from which I had occasionally suffered for a number of years; the sensation was more of a stinging or formicating nature. In most cases, the pyrogenetic or cold stage is of short duration, for soon the sensation of cold commences to alternate with one of heat, the latter predominating gradually over the former,—while a simultaneous rise of the temperature finally leads to the establishment of the hot stage.

Now, conscious of his state and confined to his bed, the patient presents an appearance of alarm and anxiety; he is restless, his face is flushed and his eyes appear muddy, owing probably to a slight œdematous swelling of the conjunctiva, produced by hyperæmia of that membrane. The tongue, at this stage, is, in many cases, found covered by a white, cream-like film, in others by a thin yellowish fur, while the point and edges remain free and are of a bright scarlet tint. As the disease progresses, the fever becomes more intense; the skin is very hot and dry; its temperature, though varying in different cases, always rising to 102–104° F. in the axilla. The pulse is full and hard, averaging from 100 to 130 beats per minute, the respiration hurried, frequently irregular. The pains in the head, back, muscles and joints of the limbs become more severe. The spinal pain, which is confined to the lumbar region, whence it may extend to the iliac portions, or to the whole of the pelvis, becomes almost intolerable, interfering with the rest of the patient, who, in seeking comfort, constantly changes his position in bed from one side to the other. Sometimes these symptoms are accompanied by gastric troubles, as nausea, and even vomiting of mucous or bilious matters, though, in general, the latter do not appear before the second or third day.

Accompanied by the above symptoms, the fever generally runs its course without abatement during the first day and night; but, severe as these symptoms may appear, there are, nevertheless, a considerable number of cases in which a favorable turn of the disease may already be observed on the day succeeding. In these cases the patient, usually after some free alvine and urinary evacuations, caused either by a simple effort of nature or by the effect of medicine previously administered, commences to perspire in the course of the night, and feels considerably relieved from his sufferings in the morning. At the same time, the pulse and temperature have considerably descended, so that before another night sets in the fever may have entirely subsided, leaving the patient in a state of nervous debility from which he may soon recover. These cases represent the *ephemeral* form of yellow fever, accompanied from its first appearance by violent symptoms, which, however, speedily subside without

leaving any serious traces behind. My own case was one of this kind.

But, in the majority of cases, the fever does not abate so soon, but continues to the third or fourth, sometimes even to the fifth day. The temperature, then, may still rise higher, to from 105–107° F., in exceptional cases even higher, while the fall of the pulse, ordinarily commencing on the second day, generally reaches the normal standard on the fifth or sixth day, and frequently even descends still lower. Gastric trouble, also, consisting in nausea, and a constant inclination to vomiting, if not present already, now commences. Generally, there is a sensation of a dull aching pain, or pressure in the epigastric region, arising from the irritation of the mucous membrane of the stomach, and caused by the now beginning hyperæmia of this organ; the nausea and inclination to vomit are also due to this condition. This painful sensation, however, is not in all cases increased when pressure is made by the hand upon the epigastrium. Still, the nausea, and the constant, often unsuccessful attempts to vomit, are very annoying, causing much suffering to the patient. If he succeed in his efforts to throw up anything from the stomach, which at this time is generally empty, the vomited matters are found to consist of a thin mucoid, sometimes ropy fluid, of a white and frothy appearance, frequently mixed with bile or small portions of undigested food; in some cases it is even mixed with pure bile, presenting, then, a green color. A microscopic examination reveals that this fluid is principally loaded with large flat epithelial cells, belonging to the scaly or squamous variety of epithelium, not derived from the epithelium of the stomach, but from that of the mouth, pharynx and œsophagus. Many of them are floating singly, but the greater part, adhering to each other in their former positions, still form small shreds of epithelium of different sizes. Others, again, are in a state of disintegration; their outlines have become faint, showing that their protoplasm is about to dissolve, resulting in the setting free of their contained nuclei and granules. It is from this source that the free nuclei and numerous granules floating in the liquid are derived. In some specimens of this frothy mucoid matter I have met with zoglœa

of micrococci, or with other bacteria; in other instances, however, these organisms were absent. In correspondence with the presence of the large epithelial cells, derived from a scaly epithelium, it will be found that by examining the fauces and pharynx, these parts, in some instances also the tonsils, are considerably congested, and I entertain no doubt that frequently the congestion extends farther down into the œsophagus. During the epidemic of 1867, I met with one particular case in which any liquid which the patient attempted to swallow never entered the stomach, but was invariably rejected before it passed mid-way of the œsophageal tube, the phenomenon depending very probably on a temporary stricture, produced by the swelling of the mucous membrane of the œsophagus; the difficulty was relieved by the application of a warm poultice. From the above examinations it may be presumed that the epithelial elements are surely derived from the congested parts, while the mucoid liquid may come from the stomach.

There are a number of cases, in which these gastric phenomena accompany the fever from its first appearance, but, generally, they manifest themselves on the second or third day. They should always be closely watched by the physician, and never be overlooked in the prognosis of the case; for the relation they bear to the final issue, in indicating the condition of the liver, as I shall show hereafter, is as important as that of the temperature, indicating the intensity of the fever.

The congestion of the conjunctiva, to which we ascribed the muddy appearance of the eyes on the first day, has now become more or less developed, giving to these organs a moist appearance. The fur of the tongue has increased in thickness, and has assumed a yellow or brownish tint. The patient is very thirsty, and constantly demands cold water to drink. This excessive thirst is usually referred to the disturbed circulation of the mucous membrane of the stomach, though I think that the fauces, pharynx and œsophagus may contribute their full share. Frequently, the water, after having remained a short time in the stomach, is thrown up again. The urine, which at first was natural in appearance, assumes now a more reddish tint, and, in some cases, it may be found to contain some albumen, even at

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this early period. The bowels are usually costive. Quite frequently the patient complains of pain in the lower part of the abdomen, directly over the region of the urinary bladder, indicating that this organ also participates in the congestion generally observed in the mucous membranes, or in other secreting organs, a condition which I have found verified in a few instances by post-mortem examination. Fortunately, the congestion in the bladder is usually slight, the pain being soon relieved by the application of warm poultices, and often followed by a passage of urine. In many cases, the perspiratory glands of the skin have now resumed their function—in some instances to such a degree as to become excessive. Sometimes the perspiration is so profuse as not only to completely wet the patient's clothes, but also the bedding upon which he rests. It is a singular fact, which attracted my notice during the epidemic of 1867, that however profuse the perspiration might be, there was no abatement in the fever observed, the temperature of the skin remained the same, or even rose, while the pulse continued to beat with the same force as before. At this time, also—sometimes earlier, but generally when perspiration commences—a peculiar odor is perceived to emanate from the patient, and, moreover, a peculiar burning, stinging sensation is imparted to the points of the fingers when the moist and heated skin is touched, as is done in feeling the pulse. I have frequently felt this stinging sensation, after I had washed my hands and left the patient. The peculiar odor emanating from the skin, and which, according to some authors, is also perceived in the breath, has been noticed by a number of physicians, and by some even been regarded as pathognomonic of yellow fever, while others have not been able to detect it. The failure of the latter, however, may be due to their sense of smell not being sufficiently acute, a circumstance rendered more than probable in consideration of the greater or lesser difference surely existing with regard to the other special senses among different individuals. I can entertain no doubt of the existence of this odor, for I have perceived it distinctly, and without a previous knowledge of it, during the epidemic of 1867 and afterward; and it is also observed by the friends and nurses of the patient. But that a particular diagnostic value should be attached to it, I

would not venture to assert in face of the fact that similar odors are perceived in other acute infectious diseases, as small-pox, scarlet fever, measles, etc. In small-pox, the odor is very distinct, and may, as I know from experience, even be perceived before the eruption makes its appearance; to myself, however, a difference appears to exist between the odors of the two diseases.

The most important clinical phenomena, observed in the whole course of this disease, are certainly those arising from the noxious influence of the specific poison upon the nervous system. In fact, the nervous symptoms are, perhaps, the first by which the disease announces its approach, and are therefore prominent among the prodromes, manifesting themselves in the form of the slight headache and the general depression already referred to. When the real disease breaks out, these symptoms become more developed, and take a part in the chill or rigor; finally, however, after the commencement of the fever, they show themselves again in the restless condition of the patient. The severe pains in the head, spine, joints and muscles, and even the occasional spasms in the latter, especially indicate a strong afflux of blood to the cerebrospinal axis, terminating, in most cases, in the establishment of a true hyperæmia, not only of the brain, but also of a portion of the spinal marrow; and, furthermore, as I shall show hereafter, of the thoracic and abdominal sympathetic ganglia. The steady progress of the hyperæmia is easily recognized by the pain in the head and spine increasing in severity, and giving rise to sighs and groans on the part of the patient. In correspondence with this condition, therefore, a slight delirium may in a number of cases be observed as early as on the first day; if not, it surely makes its appearance on the second, though it may be of a very mild character. In mild cases, it may only consist in irrational language or mutterings, uttered by the patient as he restlessly turns from side to side in a state of sleepy wakefulness; a state from which he may, however, be easily aroused when spoken to, and even return a rational answer. But, in many cases, the delirium becomes more severe, and frequently attains such a degree as to render the patient violent, necessitating the use of force to restrain him to his bed, and to protect him from injuries which he might inflict upon himself. In fatal cases, delirium is

rarely absent during the course of the disease. I am inclined to think that, with a very few exceptions, the fatality of the case always depends upon the hyperæmia of the brain.

Under these circumstances the second day and night pass away, and the third day arrives, when, perhaps in most cases, the febrile storm commences to subside. At the same time, the accompanying symptoms have also considerably abated, and the patient, greatly relieved from his pain and anxiety, feels comparatively comfortable. In many cases, however, the fever does not subside until the fourth or fifth day. Then, the above described symptoms continue with greater or lesser intensity, with the addition of others, such as temporary retention of urine, costiveness, etc. The urine, also, almost invariably now contains albumen. Frequently, the febrile symptoms commence to abate soon after a free evacuation of the bowels or bladder. With the abatement of the febrile process, the temperature also begins to fall, and the pulse, which, in most cases, commenced to fall as early as on the second day, continues its descent in the same proportion. Some slight cephalalgia, or some tenderness over the epigastric region may still exist. In favorable cases, convalescence now commences and may continue without any serious interruption, until the patient has been restored to his former health.

But, unfortunately, the disease does not run in all cases the favorable course above described. On the contrary, only too often, after the subsidence of the febrile storm, graver symptoms, more or less typhoid in character, appear. In such cases, the patient, as in those above described, though prostrated from the fever, feels, also, comparatively easy and relieved from his sufferings at the end of the febrile stage; very often the relief is so great as to induce him to think the disease has left him entirely, and that in a few days he will be able to resume his daily occupation. This condition, representing the so-called second stage, is very delusive, and may last from two to three, or twenty-four hours, sometimes even longer, when the symptoms return in another form, and the patient approaches the third stage of the disease. The fever then lights up; the temperature which had commenced to fall, may rise again; the pulse also becomes

accelerated, but instead of being strong and full, as in the commencement of the disease, it is now small and thread-like. The irritability of the stomach has increased, and is again accompanied by the vomiting of a mucoid fluid mixed with particles of food previously taken, sometimes also with flakes of black hæmorrhagic matter, or even with pure blood. The act of vomiting, however, is not performed with the same violence as before; the matters are easily thrown up. The stomach rejects anything in the shape of food or drink. At this time, also—though frequently earlier—the conjunctiva commences to present a yellowish tint, which, as the disease advances, increases in intensity. The same tint is observed in the scanty urine, which now almost invariably contains albumen. A microscopical examination of this fluid frequently shows small granular masses, and according to some authors, albuminous casts besides. The skin, especially that of the face, neck and shoulders, also assumes the yellowish tint, which, as the disease progresses, gradually extends downward over the whole body. In many instances, hæmorrhages occur from the nose and gums, and even from the ears and the conjunctiva. The tongue is generally dry, and the yellowish fur covering it during the first stage of the disease, has now assumed a dirty brownish tint; the edges, if clean, are, together with the gums, of a purplish color. The nervous symptoms are rendered more prominent; the patient becomes again more restless, and the delirium returns; but as the patient's strength is now wasted, the latter has lost part of its violence, though, sometimes, it retains its character furious up to death. Frequently, muscular spasms of the limbs and subsultus tendinum occur. As the vomiting continues, the flakes of black hæmorrhagic matter gradually increase in amount, until at last a large quantity of them, mixed with a thin mucoid fluid, and known as "black vomit," is ejected at once. Often, with the ejection of this fluid, the violence of the symptoms is reduced, and the patient, though comparatively prostrated, feels relieved from the sensation of pressure, or tightness over the epigastric region.

Before continuing our sketch of the clinical symptoms, it may be proper to first describe the microscopical character of the "black vomits." When a fresh specimen of black vomit, ejected

from the stomach of a severe case of yellow fever, is, for a short time left standing in a bottle, it separates into two parts, the one of which represents a thin mucoid fluid, while the other, consisting of its solid parts and resembling coffee-grounds, settles to the bottom of the vessel. The mucoid fluid represents most probably the water with the liquid food, previously introduced into the stomach of the patient, mixed with the mucous secretion of that organ. The solid matters of the vomit, bearing a more important relation to the pathology of the disease than the fluid, consist, besides the disintegrated matters of food, such as fat, muscular fibers, etc., mainly of the constituents of blood and epithelium. A part of these constituents of the blood is represented by a considerable number of blood corpuscles, which, however, are now deprived of their coloring material, the hæmoglobin, appearing, therefore, perfectly colorless. They are characterized by a delicate though well defined double contour, and, in some cases, have preserved their normal diameter, while in others they have more or less decreased in size. In all the numerous specimens of black vomit which I have examined, the blood corpuscles were always found colorless, without regard to their diameter. This phenomenon is easily explained in considering the facility with which these bodies part with their coloring material, when surrounded by a fluid of a lower specific gravity than that of the liquor sanguinis. The water with which the patient allays his thirst, and of which a larger or smaller quantity is almost always present in the stomach, is alone sufficient to deprive the blood corpuscles of their hæmoglobin; though it is very probable, as will be seen hereafter, that these corpuscles part with a portion of their coloring matter while still contained, in a state of stasis, in the interior of the minute vessels, and before a rupture of the walls of the latter may have occurred. The other part of the constituents of the blood, found in the vomit, consists of the free hæmoglobin, or hæmatin, presenting itself in the form of yellow amorphous patches. Generally, these patches are found in company with smaller or larger groups of blood corpuscles, or even enclosing them, from which circumstances it may be presumed, that the escape of the coloring material from the corpuscles occurred already in the interior of the vessel, and during a state

of stasis. In some specimens, the yellow patches are observed to contain minute floccules, or masses of organic granules, probably derived from the mucous membrane of the stomach. Besides these elements, a number of colorless blood corpuscles, and free epithelial cells, or their remains, are also met with.

In order to prove that these yellow patches in reality represent the coloring matter of the blood corpuscles, instead of bile, as has been stated by some observers, I filtered a quantity of fresh black vomit, and allowed the solid parts remaining behind upon the filtering paper to dry, for the purpose of applying the well known test of *Teichmann.* Accordingly, I placed a small portion of the dried material—about the size of a head of a pin—upon a glass slip, and, after rubbing it up with a trace of table salt into a fine powder, put a covering glass upon it. A drop of glacial acetic acid was then allowed to run under the latter, and the whole preparation gently warmed over the flame of a spirit lamp, until small bubbles of gas were observed to be formed. A microscopical examination, made after the preparation had cooled, showed a number of minute crystals of the muriate of hæmatin, the so-called *hœmin* crystals of Teichmann, universally regarded as the surest proof of the presence of hæmatin. In some specimens of black vomit, however, I have found hæmatin crystals already formed.

Almost in all specimens of black vomit, certain fungous growths are met with. The one most frequently found is the yeast plant, or *Cryptococcus cerevisiœ.* If the specimen is left standing, other species of fungi will be developed. Very often, also, colonies, or so-called *zoglœa of micrococcus* are observed in fresh specimens; free oscillating sphero-bacteria, however, are rarely seen, unless the fluid has been standing for some hours, or longer. Some importance has been attached to the presence of these organisms in black vomit, and attempts have been made to establish a relationship between them and the cause of yellow fever. In the beginning of the epidemic of 1867, the germ theory, which, not long before, had commenced to attract the attention of medical men, had also taken root in my mind, inducing me not only to search for the germs in the very numerous specimens of black vomit which I then examined, but, moreover,

upon the various mucous membranes of the body in the numerous autopsies which I made. Failing, however, in my attempts to discover anything in support of this theory, I did not hesitate to discard it; for, as regards the fungi met with in the black vomit, it is obvious that the germs, from which they are derived, reach the stomach with the food and drink, and with the saliva of the patient, where they undoubtedly find the necessary conditions for their development.

In continuation of our sketch of the symptoms observed in the third stage of the disease, we may state that severe and dangerous as they appear to be, and really are, they do not necessarily determine the death of the patient. On the contrary, even at this period, the disease may still take a favorable turn. In such a case, the fever, which may have lasted about twelve hours, —rarely more—gradually subsides, and with it all other symptoms assume a milder character. The skin becomes moist, the pulse falls again, though remaining very feeble and compressible. The gastric symptoms have greatly diminished, the vomiting has ceased, and only some occasional eructations may be observed. The temperature, though still above 100° F., has fallen considerably, the defervescence continuing until convalescence is established. The delirium also passes, leaving behind a moderate cephalalgia. The most prominent symptom now left is the great nervous prostration. The nervous energy of the patient has been wasted, and all that remains scarcely suffices for the ordinary supply of the various organs of the body. Nevertheless, with all this damage, the patient may rally, and with the proper nursing, and careful treatment, convalescence may be established, though, in most of these cases, it is tardy, and often accompanied by other complications, such as diarrhœa, abscesses, periostitis of the tibia, suppurative parotitis, etc. I have seen a number of cases recover after black vomit had occurred, particularly children.

If, on the other hand, no amelioration of the disease occurs in the beginning of the third stage, the symptoms above described assume a character still more grave. The temperature rises still higher, while the pulse often sinks, sometimes to rise again before death. Not only more black vomit is thrown up from the

stomach from time to time, but, in some cases, also, the same black matters are passed from the bowels. The urine becomes very scanty, sometimes suppressed for many hours—from twelve to twenty-four, or even forty-eight hours; and if voided, it is in an abnormally small quantity, and muddy in appearance. In exceptional cases, the suppression of urine lasts until death. The hæmorrhages from the nose, gums, fauces and tongue become more frequent, and others, from the kidneys and bladder, may take place, the blood escaping from the urethra. The tongue is hard and dry, covered with a brown or blackish fur, sometimes scabby; the gums are swollen, and of a purplish color, frequently covered with sordes. In many cases hiccough appears; the patient now approaches collapse.

In a number of cases, especially those terminating fatally in the early part of the third stage, the delirium remains active until death approaches. Then, the patient is very restless, constantly attempting to rise, and if succeeding, soon falls back upon the pillow, when life may be suddenly extinguished; while, in other instances, the delirium continues in a low and muttering form until death.

In cases where the third stage extends over several days, the symptoms, already mentioned, continue alternately with more or less violence until collapse sets in. The patient then breathes with difficulty, sending forth deep sighs and moans; often, his face is of a dusky color, though the whole skin has assumed an orange-yellow; his countenance is sunken, his tongue tremulous. He lies there, with dry, scabby lips, and frequently with a bloody mucoid liquid escaping from the corners of his mouth; indifferent to, or, more truly, unconscious of his condition, muttering incoherent sentences, until death relieves him from his sufferings.

The above sketch of the clinical symptoms, observed in the course of yellow fever, as it occurs in the average number of cases, I do not consider entirely complete; some additions will, therefore, be demanded to fill up the vacant spaces, though not to such an extent as to embrace all the various exceptional forms in which the disease may appear, and which mainly depend upon the age, sex, temperament, peculiar predisposition and other previously existing conditions of the patient.

Thus, as regards the temperature, it remains to be mentioned that certain regular fluctuations are observed, consisting in slight evening exacerbations and morning depressions; but, these may correspond with the diurnal fluctuations of temperature observed in health, and they cannot be looked upon as regular remissions; especially as they are equally observed in other "continued" fevers. Although during the epidemic of 1867, and at other occasions afterward, I made use of the thermometer for the purpose of estimating the intensity of the fever, it was done without regularity and system, and no notes were taken from which accurate deductions might have been made. To the extent of my knowledge, it was by *Dr. J. C. Faget*, of this city, that the first systematic observations were made regarding the rise and fall of the temperature of the body, as it occurs during the course of yellow fever; and, judging from the results of his observations, together with those of other observers, the elevation and depression of heat, and the rise and fall of the pulse during the febrile process, appears to take place after a certain type, pathognomonic to this disease. In a treatise, entitled "*The Type and Specificity of Yellow Fever, etc.*," published in 1875, Dr. Faget presents the rise and fall of the temperature and pulse—marked by dots and lines, upon systematically arranged charts—of thirty cases of yellow fever, collected and prepared by himself, Drs. *Tuatre* and *Layton;* and, furthermore, the charts of seventy-three cases, prepared from the tables of *Dr. Dudley S. Saunders*, published in his article, entitled "Observations on the Yellow Fever of 1873. Epidemic at Memphis, Tenn."* The deductions Dr. Faget made from his observations were: "That the course of the temperature in yellow fever, during the epidemic of 1870 in New Orleans, was characterized by a *single paroxysm*, the appearances of which, from one to three days in duration. was followed, without a stationary stage, by a defervescence of from four to seven days." Regarding the pulse, he states: "The maximum average being 120 pulsations on the first day; on the second day the pulse beats ten or twelve times less; in another twenty-four hours there are a dozen pulsations fewer;

* New Orleans *Medical and Surgical Journal*, May, 1873.

the *fall continues* on the following days, but with a *progressively decreasing rapidity;* in general, on the fourth day, the pulse oscillates toward eighty, and, with this figure, it has still hardly reached half of its return course, which will be completed only toward the seventh or eighth day; the descent will then go on still further, and toward the tenth day an astonishing *minimum* will be occasionally obtained; in some patients in convalescence, the pulse does not exceed forty in a minute." The average figures of the Memphis charts correspond in the main with those of the charts of Dr. Faget, and his statements, regarding the temperature and pulse in yellow fever, appear to be further corroborated when compared with the tables published by *Dr. Jos. Jones*, and prepared from his own records of ninety-three cases, and from the dates, obtained at the Charity Hospital by some of the resident students, of ninety-five cases.* Slight deviations depending on various causes, of course, may be observed to occur in different cases; yet, on the whole, the rule, laid down by Dr. Faget, seems to be true, and, if furthermore confirmed by numerous additional observations, will greatly assist in the diagnosis of the disease, even as early as the second day, when the pulse commences to fall, while the temperature rises.

Much importance has always been attached to the interruption or failure of the urinary passages during the course of yellow fever; that is, at a time when, under ordinary circumstances, they should appear. And it is not only the physician who is anxious to see the kidneys and bladder continue to perform regularly their functions, but the nurses and friends of the patient, also, knowing from hearsay the danger associated with a suppression of urine, watch the performance of the urinary function with interest and anxiety, and seldom fail to report on this subject to the physician, if he should forget to make his accustomed inquiries. Suppression of urine, it is true, is one of the most dangerous symptoms met with in this disease, and, if not relieved, will be followed by the death of the patient. But, I am inclined to think, that in many cases in which the non-appearance of the urine is ascribed to a suppression of the func-

* *Jones*—"Yellow Fever Epidemic of 1878 in New Orleans." New Orleans *Medical and Surgical Journal*, June, 1879.

tion of the kidneys, this secretion is only retained, small as it may be in quantity, in the bladder. To this view I have been led by my macroscopical and microscopical examinations of the urinary bladder and kidneys. Whenever a suppression of urine really occurs, it is always during the latter part of the third stage of the disease, and in protracted cases, after sufficient time has elapsed for the destructive pathological changes in the parenchyma of the kidneys to take place. A temporary retention of urine often occurs during the first stage of the disease, when it may depend on an irritation of the mucous membrane near the outlet of the bladder, exciting the muscular fibers of the sphincter to contraction. The relief obtained by the application of warm poultices over the region of the bladder seems to corroborate this view. If the retention occurs after the febrile stage, when the nervous energy of the patient is greatly depressed, the phenomenon may be owing to a debility, or even temporary paresis of the muscular element of the bladder itself. That such a condition may exist becomes very probable in considering the spinal hyperæmia in the lumbar region, the existence of which is not only indicated by the excessive pain in this region during life, but, moreover, confirmed by the hyperæmia, observed after death in the pia mater of the spinal marrow of the same region, extending even to the marrow itself. The details of this subject, however, I shall discuss more fully in connection with the pathology of the disease.

In regard to the "black vomit," it should be mentioned, that not infrequently fatal cases of yellow fever are met with, in which this clinical phenomenon does not manifest itself, though all other characteristic symptoms of the third stage, indicating that a hæmorrhage from the mucous membrane of the stomach must probably have taken place, may be present. An autopsy, made in such cases, will invariably reveal the presence of a larger or smaller quantity of the same black matters in the stomach; sometimes also in the intestines. The retention of these matters in the stomach during life is obviously owing to an excessive debility, not only of the muscular coat of that organ, but of all other muscles concerned in the act of vomiting, corresponding to the general nervous exhaustion of the patient.

Although our description of the symptoms accompanying yellow fever is applicable to the great majority of cases, which during an epidemic come under the observation of the physician, there are nevertheless a number of cases met with, in which the symptoms do not present themselves in the general order as above described. Such deviations from the general type, however, will always be found to depend on peculiar conditions, predispositions, or even idiosyncracies of the patient, modifying the ordinary course of the disease. To regard these various modifications as separate forms of the disease, as has been done by a number of authors, would, indeed, render the whole subject almost too complicated for the practicing physician; and it must, therefore, be left to his fundamental knowledge and sound judgment to distinguish between these forms, and, accordingly, shape his treatment. A mere distinction between a sthenic and an asthenic, or adynamic form, would suffice for all practical purposes.

A peculiar form of yellow fever, termed by La Roche the "walking grade," has been mentioned by authors, and is frequently spoken of by physicians, though I have never met with it myself. In this form, using La Roche's description, "the patient, though sometimes in bed, is found more frequently sauntering about his room; and, indeed, he at times walks about the street for recreation or business; and though, in some instances, he states that he is weak, in others he exhibits at intervals, or throughout, marks of considerable muscular strength. He complains of nothing, denies his being ill, amuses himself in reading or otherwise, and, to a casual observer, appears to be slightly, if at all, indisposed. To the physician, however, matters appear in a different light; for he may gradually observe that the patient exhibits an unusual expression of countenance—dull and listless. The eye is watery; the complexion is almost mahogany color, while the pulse is found exceedingly weak, and even totally absent. Black vomit overtakes him, even while occupied in the way mentioned, or very soon after, and death speedily ensues."

In considering the symptoms, mentioned in the foregoing description, they are easily recognized as belonging to the second or third stage of the disease; and by a closer inquiry into the

circumstances of such cases, it would most probably be found, that the patient, though really feeling ill, by some peculiar notion or caprice of his own denies this fact, while by the strength of his will he manages to walk about, and attend to his daily occupation. We may further presume, that a febrile stage has previously existed, though in a very mild form, enabling the patient to deceive himself and his friends; and, moreover, that the poison of the disease, while affecting the brain very slightly, impressed its noxious influence more upon the sympathetic ganglia, affecting the heart, liver and stomach in such a degree as speedily to interfere with the functions of life.

As a counterpart of these "walking cases," those may be mentioned in which the patient, by an extreme fear of the disease, exhausts his nervous energy, and reduces his system to a condition most favorable to the reception of the noxious poison. A remarkable case of this kind I met with in my own practice during the epidemic of 1870. It was a young man, a German, of about twenty-three years of age, who consulted me at my office, believing himself attacked by the yellow fever. By examination, I found him apparently in good health, with no symptom of any fever about him capable of detection by the touch, as the thermometer was not used. Notwithstanding, I failed in my endeavors to convince him of this fact; and my advice, to put his mind at rest by dismissing his gloomy thoughts, made no impression upon him. He left my office, and before night sent for me to visit him at his room. I found him in bed, and in the same apparently healthy condition. No symptom of disease could be discovered, but he was still deaf to the encouragement he received from his friends and myself, calculated to dispel his fears and arouse his spirit. The next day, during which he took but little nourishment, passed in the same manner; but, on the third day, fever appeared, which, however, never became excessive. On the contrary, refusing all nourishment, and evincing a considerable apathy for everything around him, he gradually passed into a lethargic condition from which no moral or physical stimulants could arouse him. On the fourth day, tenderness by pressure upon the stomach was detected, followed by black vomit and

symptoms of collapse in the evening; he died during the night in a state of coma.

Although in this case no external symptoms of the disease could be detected during the first two days, we are nevertheless justified in presuming that the poison primarily affected the mind of the patient, impressing him with the idea that something was wrong with him, and then slowly exerted its noxious influence upon the abdominal organs, and probably also upon the heart.

Another form of yellow fever, mentioned by La Roche, is the "apoplectic grade." In cases of this kind, "the patient," as this author states, "is struck down suddenly, as if by lightning, with stupor or coma, and death, preceded by convulsions, soon follows. In other instances, the progress is less sudden. Without even the slightest premonitory symptoms, the patient is in an instant seized with vertigo and confusion of mind. He complains of dull pain and fullness of the head, together with spasmodic pain and considerable debility in the legs; coldness, debility, and a feeling of uneasiness in the spinal region. The pulse varies in different cases in point of fullness and frequency, but is always weak, and finally becomes faltering. The skin is cold, sometimes dry and flabby, but generally unctuous or bedewed with cold perspiration; the stomach is sometimes irritable. In the meantime, the patient lies as if stunned, with dilated pupils, and an expression of gloom on his countenance. From this unpromising state an effort of reaction occasionally takes place, but this scarcely ever leads to a successful result. More generally, the patient becomes perfectly comatose; the eyes assume a glassy appearance, the pulse fades away, involuntary discharges and profuse hæmorrhage supervene, and death soon ensues."

In considering the symptoms of these so-called "apoplectic" cases, I cannot but think, that, perhaps in all of them, a diseased condition of the anatomical elements of the brain, especially of its minute blood-vessels, has existed previously to the attack of yellow fever. This view is corroborated by my discovery of fatty degeneration of the nuclei of these vessels in a number of patients who died from yellow fever. In face of the fact, however, that a rupture in the walls of the minute veins of the mucous membrane of the stomach really does take place in the course of this

disease, I would not venture to deny such an occurrence in the brain, giving rise to the capillary form of apoplexy. But as, to the extent of my knowledge, there is no record of apoplectic foyers discovered in the brain after death from yellow fever, I presume that the symptoms attending these "apoplectic" cases may be rather attributed to a hyperæmia of that organ, of a very high degree, together with a direct action of the noxious poison upon the substance of the cortex cerebri itself.

In viewing in this light the various forms of yellow fever, described by a number of authors, it becomes obvious that they are equally produced by one and the same poison, affecting the organism under different conditions, but always accompanied by one or more of those symptoms characteristic of the disease. None of these forms bears a peculiar, distinctly defined character; for, if this were the case, it might also be presumed that each separate form of the disease depended on a separate form, or state of the poison. Whatever, therefore, the conditions of the organism may be when attacked by yellow fever, the latter will always show its own and distinct character, expressed by its pathognomonic symptoms during life, and also by the pathological condition of the various organs, observed after death.

When yellow fever supervenes upon another pre-existing disease, it may modify the accompanying symptoms of the latter, though it will always impress upon it its own peculiar marks. In another section of this treatise, I shall speak of a case bearing upon this subject.

PATHOLOGICAL ANATOMY.

1. Condition of the Surface and Internal Organs of the Body, as Revealed by Autopsy.

As in the majority of fatal cases of yellow fever, the patient is attacked by the disease while in his ordinary condition of health, and, as in most instances only a few days intervene between the attack and the fatal issue, the dead body usually presents its natural appearance in form and dimensions. But, as regards the color, a most striking change has taken place; for the whole skin is now of a distinct orange-yellow color, even in cases where no jaundice was observed during the course of the disease. In fact, this yellow appearance of the skin is so invariably met with after death, as to have given rise to the very appropriate and characteristic name of the disease. The intensity of the color, of course, differs in different cases; but, it may be said, that it is usually proportionate to the severity of the case. Generally, it is deepest about the head and trunk, fading toward the feet, and corresponding to the manner of its progress during the course of the disease. Toward the end of an epidemic a number of cases are met with, in which the jaundice only extends to, or slightly beyond the knees. Very soon after death—sometimes even during the mortal agony—hypostatic congestions are observed, especially around the neck, shoulders and back; but, frequently also, about the face, ears, hands, feet, scrotum and penis.

In opening the *cranial cavity*, the *dura mater*, with the exception of the yellow tint which it presents, is usually found in a normal condition. In some instances, a smaller, or larger number of Pacchionian granulations, which, however, bear no relation to yellow fever, are met with. The serous fluid, contained in the arachnoid cavity, and also the surface of the brain covered by the arachnoid membrane and pia mater, present the same yellowish color. This coloration, moreover, is observed in all the tissues of the body, extent and intensity being proportionate to the severity of the case. The *pia mater* is almost always

found more or less congested. Very frequently, not only the larger and smaller veins are filled with blood, but also the cerebral and basilar arteries with their arterioles. In some cases I have found the congestion to extend over the whole of the cerebrum and cerebellum, while in others it extended more or less only over the parietal and frontal lobes; but, the pons varolii and medulla oblongata were invariably found in a state of considerable hyperæmia. The *arachnoid membrane* is frequently opaque, or even slightly thickened by exudation, and the sub-arachnoid space filled with serum. In such cases, the serous effusion has usually extended into the *substance* of the *brain*, producing an œdematous appearance of this organ. In most cases, however, the hyperæmia has extended throughout the whole of the latter, which then often appears swollen and œdematous throughout. The ventricles are then frequently found filled with a yellowish serous fluid, sometimes turbid in appearance, and the blood-vessels ramifying on their surfaces, together with the vessels of the choroid plexus, distended with blood. If the brain is cut into, the yellowish tint is observed to extend into its white or medullary substance, and the blood is seen issuing from the open ends of the cut blood-vessels. The blood-vessels of the pia mater of the cervical and lumbar portions of the *spinal marrow*, also, are found congested with blood, particularly in the latter region; in some cases, even, opacity of its arachnoid membrane is observed throughout the whole region.

In the thorax, the *lungs* generally present a normal appearance, though in some cases, smaller or larger portions of these organs are found congested, or in an emphysematous condition; other pathological changes met with do not properly belong to yellow fever. The *pericardium*, with the exception of the yellow tinge, is usually normal; but the fluid within its cavity, also tinged yellow, has sometimes appeared to be increased in quantity. In uncomplicated cases, the *heart* is generally found normal in size and form, and no changes are observed on its valves and tendinous structure, though the endocardium is frequently marked by the yellowish tint. In many cases, however, its muscular tissue, when cut, presents a pale yellowish hue, and is rather soft in consistence; sometimes to such a degree as to be

quite friable, and easily torn. In the latter instances, its reddish flesh color has entirely disappeared, and yielded to a pinkish yellow tint, indicating a high degree of fatty degeneration. In a number of cases, I met with yellow-tinged fibrinous bands, or clots of a delicate jelly-like consistence in the left ventricle; or, also, with clots of coagulated blood in the cavities of the right side of the heart.

In opening the *abdomen*, the same yellow tint is presented by the organs enclosed in this cavity; the liquid found in the latter is also frequently yellow. The veins of the abdominal viscera, contributing to the formation of the portal vein, are almost invariably found more or less distended with blood. In many cases, the congestion can be seen by the naked eye to extend into the venules of the intestines.

The *liver* invariably presents, either in parts or throughout, the characteristic pale yellow appearance, indicating fatty infiltration or degeneration. In former epidemics, I have met with a number of cases in which this yellowish appearance was only presented by larger or smaller portions of this organ, while others presented a bluish color, indicating a simple congestion; and again, smaller portions were observed to have retained their normal appearance. Moreover, when the organ was cut and pressed, small drops of bile were, in some instances, still observed issuing from the cut ends of the biliary ducts. During the epidemic of 1878, however, the fatty infiltration generally extended throughout the whole liver, often to such a degree as to render the parenchyma of the organ quite friable, and easy to be torn. In a limited number of cases, this organ presented more or less the well-known "nutmeg" appearance, while in others the congestion appeared to be confined to the "inter-lobular vessels."

The *gall bladder* contained, in almost every case, a greater or smaller quantity of a dark-brown, or black tar-like bile; its walls were thickened by œdema. Only in those cases in which the fatty infiltration had not extended throughout the whole liver, have I observed the bile of a lighter brownish color, and in a perfectly fluid condition.

The *mucous membrane* of the *stomach* presented in the thirty cases which I examined during the epidemic of 1878, more or

less that peculiar form of congestion, to be described hereafter; and with only one exception, the stomach itself was found to contain a larger or smaller quantity of black vomit. In the exceptional case the patient had vomited the black fluid shortly before he died. As regards abrasions, or actual lesions of the mucous membrane of this organ, I have failed to discover any during the last epidemic, nor can I remember to have observed some in the cases which I examined in former epidemics. In only one case during the epidemic of 1878, I observed a black spot of an oval form, about 5 by 4 mm. in extent, in the mucous membrane, presenting a gangrenous appearance. On a closer examination, however, this proved to be an extravasation of blood into the tissue of the membrane, and not an actual lesion; its surface being smooth and on the same level with the rest of the membrane. The color of this membrane, of course, depends on the extent and degree of intensity of the congestion; though in those parts free from the latter it is generally normal in appearance. In those cases which I examined previously to 1878, I remember to have met with some in which the mucous membrane of the stomach presented but slight traces of congestion, and was unusually pale, but not friable, as has been stated by some authors. I cannot but think that the friable condition observed by the latter, was owing to post-mortem changes.

The *spleen* presents, in the great majority of cases, a normal appearance, and when cut its pulp assumes a scarlet hue. Only in exceptional cases did it appear enlarged, or did its pulp preserve its original dark, reddish-brown color.

The *kidneys* usually present a more or less abnormal appearance, both in consistence and color, though of normal size. In a few instances only I have observed them slightly enlarged, and softened. When a longitudinal section is made through one of these organs, it is found that the medullary substance, represented by straight tubules only, has preserved its flesh color, while the cortical substance has assumed a more or less yellowish tint. In a considerable number of cases, however, this tint does not extend throughout the whole organ, for there are certain portions left presenting an almost normal appearance. In fact, I have met, during the last epidemic, with cases in which the kid-

neys appeared entirely normal, so that in some instances I did not care to preserve them. In certain other cases during previous epidemics, I have observed the kidneys in a high degree of congestion, marked by a bluish-red color throughout. I have never met in yellow fever with the so-called "large white or smooth kidney," characteristic of parenchymatous nephritis.

The condition and appearance of the *supra-renal bodies* will be described in the following parts of this treatise.

The *urinary bladder* is generally found in a normal condition; in a few cases only I have observed traces of a slight hyperæmia in the mucous membrane, near the outlet of the organ. In about one-half of the cases examined in 1878, I found it still to contain a smaller or larger quantity of urine, and in one case it was even found distended with this fluid.

A peculiar slightly pungent odor, similar to that arising from the perspiration of the living patient during the course of the disease, may also be observed to arise from the interior of the dead body, while it is still warm, and when its cavities are opened, or when the muscles are laid bare and extensively cut into, as is done in removing the spinal marrow from its canal. This odor, like that arising from the body of the living patient, has at all times been perceived and mentioned by a number of physicians performing autopsies, while others have failed to detect it. The failure of the latter, however, may either have depended on a certain dullness of their olfactory sense, as once mentioned before, or upon their autopsies having been performed at a time when the body had entirely parted with its heat. In my own cases, the autopsies were made from three-quarters of an hour to three or four hours after death; in only a few instances the time extended to five or six hours. I am the more convinced of the existence of this odor, as I have compared it with the ordinary odor arising from the dead bodies of cases dying from other diseases, and on which the autopsy was performed at the same time.

The above description of the condition of the organs of the dead body in fatal cases of yellow fever, as revealed by macroscopical examination, relates in particular to the thirty autopsies which I carefully made during the epidemic of 1878; and, fur-

thermore, to others almost as numerous, and performed at the Charity Hospital during previous epidemics, either by myself or by the surgeon or resident students of that institution.

2. Pathological Changes, Occurring in the Tissues of the Organs during the Course of the Disease, and Revealed by Microscopical Examination.

The pathological changes produced in the tissues of a number of organs by the direct or indirect action of the noxious poison of yellow fever, are, individually considered, by no means pathognomonic of this disease. On the contrary, they are equally observed in other diseases, whether infectious or not, in which the nutrition of the system has been disturbed and deranged, either by the interference of an infectious poison, or by the abnormal performance of the function of one or another organ. It is, therefore, only when considered as a complex, and in association with the clinical, phenomena, that these changes may receive a pathognomonic significance. But, even, without regard to this significance, the exact knowledge of these changes is so highly essential to the knowledge of the true nature of the disease, as to render the importance of their microscopical study obvious to every physician. For this reason, I shall, in describing the pathological condition of the organs, as revealed by a close and accurate microscopical examination, enter more into the details of the subject than I have done in the preceding part of this treatise, in which the object in view was to combine exactitude of description with brevity of communication. And as this treatise is intended to be read, not only by the accomplished physician, but also by the medical student, as yet not thoroughly familiar with the more minute studies of anatomical science. I deem it practical to draw a brief sketch of the normal histology of the respective organs, before describing the pathological changes which they undergo during the course of the disease.

I shall begin with that most important and interesting tissue, the blood, which, partly solid, partly fluid, receives all matters, essential to the maintenance of the life of the body, and which,

in distributing them to all its parts, represents the most important factor in the process of nutrition. But, while it thus receives and distributes the materials essential to the normal condition of the organism, it is also capable of receiving noxious substances, such as infectious poisons, from the surrounding air, which, in disturbing the process of nutrition by their deleterious influence, give rise to pathological phenomena, characteristic of the disease under discussion. The condition and behavior of the morphological elements of this liquid tissue in a number of diseases have of late formed a special subject of research and discussion, and have given rise to many contradictory statements and views. It is therefore desirable for the medical practitioner to be acquainted with the leading facts of this subject, to enable him to form an opinion of his own.

THE BLOOD.*

The colored blood corpuscles of man represent, like those of other mammalia, minute bi-concave disks, the mean diameter of which ranges, according to the very accurate measurements of *Woodward*, from .00731 to .00772 mm., though in some specimens I have observed them slightly larger. They are very delicate in substance, and being elastic and flexible in an unusually high degree, are enabled to resume always their original form when distorted by mechanical causes. In fact, the momentary changes of form, which they are constantly undergoing when floating in the liquor sanguinis, are owing to the great delicacy and elasticity of their protoplasm. In examining them under the microscope with a sufficient amplification, we observe that the most feeble current arising in the liquid in which they float, disturbs their form, either directly, or from mutual contact or pressure. When a colored blood corpuscle of man is examined in a state of rest from the front, its outline appears perfectly round. Bring it into proper focus, so that its outlines appear the most distinct, its center, to the extent of about one-third of the whole diameter appears light. Proceeding toward the periphery of the corpuscle, a slight shade is seen to arise from the light center, which,

* A portion of the following description of the morphological elements of the blood will be taken from my last paper on this subject, embodying my own researches, viz.: "The Structure of the Colored Blood-corpuscles of Amphiuma tridactylum, the Frog and Man," published in the *Journal of the Royal Microscopical Society of London*, 1878.

after increasing somewhat in depth, is gradually lost, to be followed by the high light, representing the convexity of the margin. This variation of light and shade is, of course, caused by the form of the corpuscle. The convex margin appears most illuminated at the highest part of the convexity, when the rays of light passing through it undergo very little refraction, while more or less shade must appear, by virtue of the refraction of light, at that part of the surface which inclines toward the center, and forming a part of the concavity; the center, finally, being the thinnest portion of the corpuscle, and very nearly flat, must, from the absence of almost any refraction, appear light. Owing to the rounded margin of the blood corpuscle, its very outlines do not appear distinct and sharply defined; on the contrary, a delicate shade is observed at the very edge, which soon disappears in the high light of the convexity. No trace of the existence of a membrane, or a membranous layer can be discovered in the fresh blood corpuscle of man. When brought into exact focus, it appears encircled by a narrow ring of a pinkish tint, much lighter than the rest of the surrounding liquor sanguinis; this phenomenon is probably owing to the corpuscle refracting the light towards its less refractive medium. The appearance of the colored blood corpuscle of man in exact profile is peculiar, and corresponds not to the bi-concave form in which it is so often erroneously represented. Recollecting that its body represents a minute plate or disc, the peripheral portion of which, besides being convex and rounded at its border, is twice as thick as the central, which is concave; and further, that it is perfectly symmetrical at all points, it becomes evident that the outlines of its profile must be represented by two *straight* and *parallel* lines, connected at their extremities by two semicircular ones; and accordingly the side-view of the corpuscle could not reveal the concavity of the central portion. But, if a vertical section were made through the center of the corpuscle, the outlines of the cut surface would be represented by two slightly curved lines, which, directing their convexity toward each other, are connected by semicircular lines, the whole showing not only the bi-concave form of the central, but also the convex and rounded form of the peripheral portion of the body.

The color of a single blood corpuscle when seen under the microscope is not yellow, as has been stated sometimes, but more of a light greenish tint. It is only when a number of blood corpuscles are collected into a small mass or group, and rest upon each other, that the original greenish tint merges into a yellow. With the increase of the thickness of the mass, the yellow becomes darker, and finally passes into the scarlet red, as seen in a drop of blood.

Soon after a small drop of human blood has been put on the glass slide and covered with the plate of thin glass, a number of blood corpuscles are observed to change in various manners, and in a slighter or greater degree, their original form. In some instances the convex peripheral portion of the corpuscle appears to shrink in thickness at one point, while the rest of it swells and gains in diameter, so that the whole body assumes a wedge-like form. In other instances the blood corpuscle assumes the form of a shallow basin, an appearance which is very probably caused by a contraction of the convex border of only *one* surface, by which process the concavity of this surface increases in depth, while the other surface is rendered convex instead of concave. If the contraction continues, the corpuscle assumes the form of a deep cup. Whether during this process the central portion increases in thickness, while the convex periphery is rendered thinner by the contraction, is difficult to determine; but that the contraction takes place only on *one* surface of the convex margin is obvious, for, if it occurred throughout the whole margin, the corpuscle would not become cup-shaped, but would preserve its original form of a disc, though its central portion might gain in thickness, while the concavities of its surfaces would decrease in depth, or entirely disappear. Sometimes the convexity of these cup-shaped forms terminates in a conical protuberance. There is another very singular form observed, difficult to describe, but resembling in some respects the wedge-like form, with the exception of the narrow portion of the wedge; instead of being straight, assuming here the form of a Y, showing that the body must be three-sided.

Intermediate forms, similar to those above described, are observed; but it will be noticed that in all these instances it is only

a portion of the protoplasm of the blood-corpuscle which is contracting, while the rest is expanding in compensation of the contraction. There are, however, other changes occurring in the form of the corpuscles, owing to a contraction of the protoplasm throughout the whole body, and accompanied by a considerable diminution in size. As the result of such a contraction we may regard those familiar forms of blood corpuscles, generally compared to a mulberry or thornapple. These, when occurring on the blood corpuscle of fresh blood, and without the action of a reagent, have generally been attributed to the evaporation of the liquor sanguinis. With the increase of the density of this liquid, namely, an exosmotic current from the blood corpuscle is supposed to be induced, causing shriveling of these bodies. If this view were correct, those corpuscles nearest to the edge of the film or layer of blood under the covering-glass, should first undergo the changes in question. But this is not always the case; on the contrary, single mulberry or thornapple-shaped blood corpuscles are observed among the mass of unaltered ones in the center of the preparation, immediately or soon after the blood is placed on the slide. Soon after, other individual corpuscles are seen to assume these forms, the number increasing with the time, until finally whole groups or the entire mass may undergo this change. In other instances, considerable portions of the blood corpuscles of the preparation may, soon after the blood is put upon the slide, contract at once, and assume the thornapple form, appearing almost as if affected by a general contagion. The thornapple form may even be produced by the action of water, as I have observed. The form of the blood corpuscle, when gradually and slowly undergoing these changes, seems to pass through several phases. The first deviation from the original form observed consists in minute elevations and protuberances, arising from the surface of the corpuscle at its rounded margin, thence, while increasing in number, extending over the entire corpuscle. Next, the protuberances, at first of a conical form, become gradually smaller in diameter at their base, while their points or summits enlarge to assume the form of an imperfect knob, resembling a granule. It is at this stage of the change that the form of the blood corpuscle has been compared to that of a mulberry. As

the change continues the globular projections become thinner, until finally they are transformed into minute, sharp, spinous processes. In this state the blood corpuscle resembles a thornapple. But it is not necessary that, when the change of form has set in, it should pass through all the stages to the ultimate thornapple form; on the contrary, the contraction may cease at any stage of the process, or even cause at once the mulberry or thornapple form. Very little alteration in the general form of the corpuscle is observed to take place by this process; it is not rendered spherical, as might be supposed, but represents still a disc, though the concavities may have disappeared from its surfaces, or even be converted into convexities.

The colored blood corpuscles of man are also endowed with the power of spontaneous motion, protruding and *retracting* minute processes similar to those observed on the thornapple form, a phenomenon which I first discovered in the summer of 1871, and which shows that these bodies not only possess a certain inherent power of contracting their bodies, but also of resuming their original form by a subsequent expansion, a characteristic property of the living protoplasm, enabling the corpuscle to manifest these motions, though not to so great an extent as is seen in the colorless. Keeping in mind this inherent property of the colored blood corpuscles, a part of the difficulty hitherto encountered in tracing these various spontaneous changes, occurring in the form of these bodies, to their cause, will be removed.

Nevertheless, as these changes are not only observed to occur in different localities of the same preparation of blood, and under different circumstances, but, moreover, are observed to occur in a greater or less degree in different specimens of blood taken at different times from the same individual, much doubt will still remain as to the true cause of the phenomenon, and the conditions under which it is manifested. The question, therefore, arises: Do these changes of form indicate progression and development, and a high degree of vitality residing in those blood corpuscles exhibiting them, or do they result from a loss of vitality, and are they manifestations of retrogression and decay? In the one case, they would probably occur on the young, in the other on the old corpuscle.

If the changes affecting the form of the colored blood corpuscle, and evidently caused by a contraction of its protoplasm, were indicative of a higher degree of vitality or molecular action, we should meet with a greater number of mulberry or thorn-apple-shaped, or otherwise deformed corpuscles in the fresh blood. But as, on the contrary, the number of these forms is comparatively small, immediately as the blood is removed from the living tissues, and, moreover, increases sometimes quite rapidly in proportion to the length of time intervening, it appears more probable that these changes of form indicate retrogression, and we may be justified in regarding them as the result of the last vital action manifested by the blood corpuscle, and portending its death.

When a very small portion of human blood is spread upon a glass slide, and after being covered by a thin plate of glass, a drop of water is added to the preparation, it will dilute the liquor sanguinis and induce an immediate escape of the hæmoglobin from the blood corpuscles, rendering the liquid in the vicinity of the latter, according to their number, more or less turbid. At the same time the blood corpuscles will be set in motion, and float away in the clearer parts of the liquid. Continuing to part with their coloring matter, they are gradually rendered pale, and finally appear as mere shadows. If now a portion of the liquid is removed by the careful application of a minute point of a piece of blotting paper, and its place filled by a small drop of clear water, the shadow-like blood corpuscle—if examined by a first-class objective—will appear bordered by a delicate double contour. The central portion of the corpuscle, encircled by the inner contour, appears now of the color of the field, while the margin, included by the two contours, appears lighter when put into the exact focus. This double contoured margin represents the outer portion of the protoplasm of the colored blood corpuscle forming the surface, which is denser in its molecular constitution than the rest of this substance, enabling it to withstand the solvent action of the water, endosmosing into the interior of the blood corpuscle, while the rest of the protoplasm is discolored, and perhaps dissolved, or otherwise affected by the action of this fluid. In the fresh and unaltered condition of the blood corpuscle of man, this denser portion of the protoplasm, forming a very thin layer on

the surface of the latter, cannot be demonstrated, having the same index of refraction as the rest, but by the action of water, or of solutions of certain other reagents, it becomes visible in the form of an artificial or pseudo-membrane, for which reason I have named it the "membranous layer" of the blood corpuscle.

The changes produced in the colored blood corpuscle by the action of water are equally observed when these bodies are treated by a number of other reagents, both in liquid and gaseous form; they mainly consist in the escape of the hæmoglobin, contraction or coagulation of the protoplasm, and change of form. The action of the chloroform vapor particularly is very rapid in causing the escape of the hæmoglobin, though it does not dissolve the corpuscles as has been stated.

As regards the colorless blood corpuscles of man, it may be stated that they consist of a pale, finely granular protoplasm, inclosing, in most instances, one homogeneous disc-shaped nucleus, though sometimes two nuclei are observed. In the fresh blood, a considerable difference exists in the size of these corpuscles. In the protoplasm of the larger corpuscles, a group of dark-bordered granules, much larger than those properly belonging to the protoplasm itself, and rather similar to the pigment granules of the gangloin cells of the nervous centers, are observed. If a specimen of blood is examined fresh, and under the proper condition, these dark granules may be observed to perform certain oscillating movements, while the pale granules of the protoplasm also exhibit a constant motion, though more rotary or molecular in kind, and not as active as that of the former. Besides these movements of the individual granules—which seem to be identical with the well-known "Brownian movements" of minute particles—there are the so-called amœboid movements, in which the entire protoplasm of the colorless blood corpuscle takes part, consisting in a continuous change of form by the alternate projection and withdrawal of larger or smaller processes, resulting in locomotion. The amœboid movements of the protoplasm are not regularly observed to take place on all colorless blood corpuscles of the same specimen of blood; according to my own observations they appear to occur more rarely in the smaller individuals than in the larger. In some cases, these movements appear im-

mediately after the fresh drop of blood is put upon the glass slide; in others, again, only after the addition of some water or slightly alkaline solution, or the application of warmth. In the fresh unaltered condition no enveloping membrane can be discovered on these corpuscles, but by the action of water I have frequently observed them bounded by a very delicate double contour. The proportionate number of the colorless blood corpuscles to the colored is very small, and varies in the blood vessels of different parts of the body of the same individual, as well as at different periods of the day. In the normal condition of the blood, the proportion has been estimated to be one colorless to two or three hundred colored blood corpuscles.

Besides the above described blood corpuscles, an insignificant number of very minute colored corpuscles are met with in many specimens of normal human blood. The diameter of these bodies ranges from hardly one-third to two-thirds of that of the ordinary colored blood corpuscles. They have been called "microcytes," and regarded as younger individuals; a view corroborated by my own observations on the development of the colored blood corpuscles in the human embryo, where many of them are met with in the blood as late as the third and fourth month of embryonic life.* The same view is taken by *Hayem*,† who met with the smallest forms of these bodies, $\frac{2}{1000}$ mm. in diameter, always under conditions where a new formation of colored blood corpuscles might be supposed, as in new-born children, menstruating women, after losses of blood, or in feeble individuals. I have frequently observed these minute corpuscles having assumed the thornapple form.

Independent of these minute colored corpuscles, however, not unfrequently other elements are met with in normal blood, not larger than minute organic granules, and colorless. They have been seen and described under different names by different observers, and have been generally considered to be derived from the granular protoplasm of the colorless blood corpuscle. When first known as the "elementary bodies" of *Zimmermann*,‡ who had demonstrated them in salted blood, they were regarded

Monthly Microscopical Journal, February, 1874.

†*Virchow u. Hirsch*, Jahresbericht fuer das Jahr, 1877, Vol. I., p. 38.

‡ *Rollett*,—Stricker's Handbuch der Lehre von den Geweben, etc., p. 300.

as the colorless remains of disintegrated colored blood corpuscles (Henson), and to be identical with the granular formations, previously met with in the blood by *Max Schultze; Béchamp* and *Estor*, who also observed these granular elements in the blood, called them "microzyma;" and, observing under the microscope a colored blood corpuscle breaking up into a number of these microzyma, while, on the other hand, they also observed a number of these elements aggregating and forming a colorless blood corpuscle, they concluded that all blood corpuscles represented aggregates of microscopical organisms.* Elements, identical with the above, were moreover mentioned by *Bettelheim* and *Lostorffer*. Under the name of "hæmococci," they were subsequently described by *Nedsvetzki*† as minute round bodies, resembling the granular particles of the colorless blood corpuscles, and forming normal constituents of human blood, becoming very distinct with an amplification of from 900 to 1,000 diameters, and found in large numbers among the colored and colorless corpuscles. In the dead colorless blood corpuscles, he observed molecular motion to take place, and, furthermore, the formation of a light zone around them, into which the minute granules entered, and thence passed into the liquor sanguinis, where they continued their movements in the same manner as in the hæmococci.

At present, there remains no doubt but that all these granular elements, met with in normal blood, and named differently by different observers, are derived from the finely granular protoplasm of the colorless blood corpuscles, and the movements they may exhibit are simply "Brownian" in their nature. I have frequently met with protoplasmatic remains of colorless blood corpuscles in human blood; and, a number of years ago, in the case of a man poisoned by cyanide of potassium, I observed, eight hours after death, a number of these amœba-form masses of protoplasm without nuclei, in which the minute pale granules were still in active motion; which continued for a considerable time after the addition of water to the preparation.

Having, by the above sketch of the anatomical elements of the human blood, prepared the way for the description and discussion

* *Virchow u. Hirsch*, Jahresbericht f. d. Jahr 1870, Vol. I, p. 18.
† l. c.—für das Jahr 1873, Vol. I, p. 50.

of the condition and behavior of these elements in yellow fever, I shall now return to the original subject. The specimens of blood which I examined during the epidemic of 1867, were obtained from hæmorrhages from the nose, occurring on some of my patients. The blood was collected in small vials, and a limited space of time, of course, elapsed, before I could examine it at my office. The microscopical examination of these specimens showed that the greater portion of the colored blood corpuscles had assumed the thornapple form, but I was unable to detect any other abnormal condition of these bodies, nor any foreign body in the specimens. In other specimens—taken during the same or succeeding years—after death from the larger superficial veins of patients at the Charity Hospital, I was also unable to detect anything foreign to this liquid. The blood corpuscles, in general, exhibited the same characters and phenomena as those of healthy blood under the same conditions. Only in one case, I observed some phenomena on a small number of colored corpuscles, which, at that time, I was unable to explain satisfactorily to my mind. These blood corpuscles, namely, presented two or three *apparent* openings, or, better said, solutions of continuity upon their surfaces, manifesting themselves by a bright light-pinkish color. From what I know at present, this phenomenon must have been owing to the presence of minute vacuoles in the protoplasm of the corpuscles, such as I, sometime afterward, discovered on a large scale in the giant blood corpuscles of *Amphiuma tridactylum*. On some other colored corpuscles of the same specimen, I observed the membranous layer of the corpuscle separated from the rest of the protoplasm, a phenomenon which I also subsequently observed on the colored blood corpuscles of the frog. As, in these cases, the blood had been taken from the dead body, it is obvious that the phenomena observed were owing to the post-mortem changes, for which reason I attached no importance to the observation.

During the month of August, in the midst of the epidemic of 1878, I made, more systematically than before, a series of examinations of the blood of living patients at the Charity Hospital. They were made in the following manner: The microscope being placed near one of the windows of the ward for the purpose

of obtaining the best light, and with everything required for the examination, such as glass slips, covering glasses, etc., in perfect order and readiness, I went to the bed of the patient, and to obtain the blood made a small incision into his forearm. Knowing from my former researches upon the normal blood that the colored blood corpuscles of the first drop, issuing from the capillaries of the skin, are more liable to changes of form, when placed upon the glass slide, than those coming from deeper parts, I took the precaution of making no use of the first drop, except in a few instances. For this reason, the skin was again cleanly wiped, and a small portion of the blood next appearing in the incision quickly—at the bedside—placed upon the glass slip, and covered with a very thin and small cover glass. As soon as covered, it was put upon the microscope for examination.

Previous to these examinations of the blood of the living patient, I had observed in some sections of liver and of some other organs, taken from yellow fever cases, extravasations of free hæmoglobin from the capillary vessels, and its absorption by the surrounding cells; and, in accordance with this observation, I somewhat expected to meet with free hæmoglobin in the blood itself, supposing its escape from the colored blood corpuscles to be caused by the action of the specific poison of the disease upon the latter. And, by coincidence, I really found in the first specimen which I examined some of this coloring material, which, however—as must be remembered—is a phenomenon not unfrequently met with, even, in the examination of normal human blood. In this specimen, moreover, I observed that the greater portion of the colored blood corpuscles presented mulberry and thornapple forms, while the rest was rapidly assuming them. In all other respects, with the exception of a few microcytes, the blood appeared perfectly normal. *Not a single bacterium, or spore of a fungus*, was I able to discover, though I honestly endeavored to do so. In the next specimen of blood which I examined, and which was obtained from the same patient and from the same incision, I did not even meet with the free hæmoglobin. But, as in the first specimen, in this also, the greater portion of the colored blood corpuscles had already assumed the

mulberry or thornapple forms when first seen under the microscope, while the rest was undergoing these changes quite rapidly.

In this manner I examined the blood of *fifteen* living patients, representing the different stages of the disease: that is, from the second day to one-half hour before death, or to convalescence. Two specimens of blood were examined in each case; in some even as many as three or four, but on different days. In all the cases, with the exception of two, the blood corpuscles presented the mulberry and thornapple forms, adhering frequently to each other in the form of rolls, forming irregular anastomoses. In a number of these cases the blood corpuscles had already assumed these forms and arrangement when first seen under the microscope; this was decidedly the case in a specimen of blood taken from a patient during the agony of death. In the two cases of exception, the colored blood corpuscles presented an appearance as normal in form and character as I ever beheld. and, moreover, retained it for a considerable time. The patients here were both Germans; the one, a boy, of 15 years, who had arrived at New Orleans by an English steamer three weeks before he was taken with the disease; his blood was examined on the fourth day, during the second stage of the disease; he recovered. The other was a strong and hardy young man of 22 years, a gardener, who had arrived from Germany during the month of February, 1878; his blood was examined on the second day of the disease, when he was very restless and slightly delirious; he died on the fifth day.

As regards the colorless blood corpuscles in the specimens of blood taken from the above-mentioned fifteen patients, nothing specially abnormal could be discovered. In one specimen only, taken from the blood oozing from a slight wound of the ear of a patient, and during the second stage of the disease, the relative number of these corpuscles appeared to have slightly increased, and amœboid movements were observed on some of them. In the other specimens, most of the colorless corpuscles observed belonged to the smaller kind, performing no amœboid movements, their number being, as far as I could judge, in a normal proportion to the colored blood corpuscles.*

*The results of my examinations of the blood in yellow fever have been corroborated by

Two specimens of blood, obtained two hours after death, for the purpose of determining the relative quantity of fat they contained—the one from the portal vein, the other from the right side of the heart—were also examined. They presented nothing remarkable. A portion of the colored blood corpuscles had assumed the thornapple form, while the rest had preserved their natural appearance; they were adhering to each other, forming rolls, no bacteria or fungi-spores were met with.

In reviewing now the results of my numerous examinations of the blood, it must be admitted that the condition in which its morphological elements were found, actually offers nothing remarkable, or otherwise, which in any way could be interpreted as peculiar or characteristic of yellow fever. The only conclusion to be drawn from these observations is, that the colored blood corpuscles of yellow fever blood are strongly inclined to assume the mulberry and thornapple forms as soon as removed from the circulation, indicating, in accordance with the view I have previously expressed, a certain loss of vitality. But the significance, which this phenomenon might appear to have in connection with the particular nature of yellow fever, is lost when we consider that the same behavior of the colored blood corpuscles has been noticed in the blood of patients laboring under other febrile infectious diseases by a few observers, though others fail to mention it. Thus, *Laptschinsky** found in his histological examinations or the blood of patients, suffering especially from febrile infectious diseases, that the colored blood corpuscles formed no columns of so-called money-rolls, but aggregated in masses and lumps of different sizes and form. The individual blood corpuscles frequently appeared as if swollen and turbid, their contours being less distinct. In such cases, he also frequently met with very minute blood corpuscles, adhering to each other quite tenaciously in the form of small aggregates. The colorless corpuscles, also, appeared increased in number, their amœboid movements were distinct, and extended upon the nuclei.

Dr. Sternberg, who examined a considerable number of specimens in the Military Hospital at Havanna in 1879, without discovering any bacteria, or other minute organisms, in the fresh blood. Regarding the colorless blood corpuscles, however, he met in several cases with some which presented fat globules in their protoplasm, a phenomenon which finds a satisfactory explanation in the fatty infiltration of other organs.

**Virchow u. Hirsch*, Jahresberischt f. d. Jahr. 1874, Vol. I., p. 339.

Thus far, then, no particular value should be attached to the fact that, with a few exceptions, the colored corpuscles of yellow fever blood assume the mulberry or thornapple form quite rapidly after their removal from the circulation; the significance of this phenomenon should be regarded as of secondary importance. Although I presume that the cause of this unusual tendency of the colored blood corpuscles to assume these abnormal forms is probably due to a loss of vitality by the pernicious influence of the infectious poison, I do not attribute the final effect to this cause alone, but, on the contrary, rather consider their removal from the living tissue, together with the exposure to the atmosphere, as the main factors concerned in the whole phenomenon. The loss of vitality renders the blood corpuscle more sensitive to the influence of these factors, which, in its healthy condition, it might have resisted for a limited space of time. In a number of specimens of blood, taken from the living patient, a portion of the colored blood corpuscles, as above mentioned, had already assumed these abnormal forms when first seen under the microscope; an observation which might lead to the supposition that they had undergone this change while still circulating in the blood vessels. I can safely assert that this is not the case, for I do not remember that in the numerous thin sections of all parts of the brain and other organs, which I have made and examined, and in many of which—especially in those of the brain—all the minute blood vessels are filled with blood, I have ever met with mulberry or thornapple-shaped blood corpuscles. And, moreover, in order to satisfy my mind on this particular point of the subject, I have lately re-examined a very considerable number of thin sections of the brain, sympathetic ganglia, and some other organs, and obtained the same results.

But though we may not attach any pathognomonic value to these almost constantly occurring morphological changes in the colored blood corpuscles in yellow fever, they may nevertheless be regarded as a result of the febrile process in general. Of late years, quite a number of observers have directed their attention, not only to the relative proportion of the morphological elements of the blood to the liquor sanguinis, or to the relative number of the colored and colorless blood corpuscles themselves, in various

diseases of the blood, but, moreover, to the morphological changes to which these bodies are liable in different diseases. The extreme sensitiveness of the blood corpuscles to extraneous influences, however, renders it in many cases difficult to determine whether the changes observed are due to the latter, or to real morbid causes; therefore, the investigator should be perfectly familiar with the morphological changes observed in normal blood, and not be endowed with a too vivid imagination.

As regards those minute colored corpusles, the so-called "microcytes," the proportionate number of which in normal human blood is 1 to 2000 of the ordinary colored blood corpuscles, they may also increase in number in certain diseases of the spleen and liver. *Vanlair* and *Masins** met with an extraordinary case of this kind, in the blood of which (a woman) they found the number of the microcytes increased to such an enormous extent, as to have only two colored blood corpuscles to 100 microcytes. This case induced the authors to apply the particular name of "microcythæmia" to this affection.

Those minute granular colorless elements, the "microzyma" of Béchamp, resulting from the disintegration of colorless blood corpuscles, may also, under certain pathological conditions, be found increased in quantity in the blood. They have not unfrequently been found, as well in febrile as in non-febrile diseases, and may give rise to very serious errors, by being mistaken for bacteria. I am much inclined to think that the statements of some physicians, relating to the presence of bacteria in yellow fever blood, were based upon such observations; or, if the bodies observed were bacteria in reality, they certainly entered the blood sometime after it had been removed from the living or dead body.

THE HEART AND LUNGS.

The observations upon these organs worthy of any remark, have already been made in the section treating of their condition as revealed by the autopsy. As regards the heart, it may be added that in those cases in which a fatty degeneration of this organ exists, the degenerative process is very rarely observed to have extended throughout the entire organ, but is mostly found

*L. c.—fuer das Jahr, 1872, Vol. I., p. 201.

limited to certain portions. The process itself does not consist in a mere infiltration of fat, as is met with in the liver, but in a true fatty metamorphosis of the muscular fibers. As fatty degeneration of the muscular tissue of the heart, however, not unfrequently takes place during the course of other infectious diseases, such as typhus, etc., and even in some other diseases of a chronic character, it cannot be regarded as pathognomonic of yellow fever.*

The *lungs* are, as has been already stated, generally found in a normal condition. In a few exceptional cases, small portions of them are found in a congested, or, also, emphysematous condition. But in consideration of these changes being observed but very rarely, they should be regarded as of an accidental origin, bearing no special relation to yellow fever. It is rather the immunity from the noxious influences of the yellow fever poison which these organs manifest, that may be considered as a characteristic feature of the disease.

THE LIVER.

The pathological changes occurring on the parenchyma of this organ, are so invariably met with in fatal cases of yellow fever, that they may safely be looked upon as a pathognomonic feature of the disease; and they should, therefore, be studied with the greatest care and attention. The close relationship in which the liver stands through its portal circulation with other abdominal organs, renders the latter liable to be involved in almost all the disorders of the former, a complication very frequently occurring in yellow fever. In such cases an approximate idea of the condition of the liver is easily obtained by observing those clinical symptoms indicating the condition of the stomach and intestines, and which may prove of service in the prognosis of the case; for it may well be presumed that the general condition of the patient

* In the report of the "Havanna Yellow Fever Commission of the National Board of Health," it is stated: "that there is no foundation for the opinion that there is a fatty degeneration of the muscular fiber of the heart in yellow fever." This assertion can only be explained upon the supposition that the hearts examined very singularly *happened* to belong to such cases in which the fatty degeneration of this organ was really absent, as it is hardly probable that the type of the "yellow fever at Havanna" should so much differ from that of New Orleans; or that the expert who made the examinations, could have failed to recognize this well-known pathological fact, observed in many cases of this disease.

very nearly corresponds to the extent of the pathological changes taking place in the liver. Thus it is, that in most fatal cases of this disease, the pathological changes revealed by the macroscopical and microscopical post-mortem examinations in the liver, are almost always found to exist in a high degree, a circumstance which leaves little opportunity to the pathologist of studying the initiary stage of the pathological process.

From the hyperæmic condition in which a number of the other organs of the body are found after death, it may also be presumed that the pathological changes observed in the liver are likewise preceded by a state of congestion. Although in all the cases which I examined during the epidemic of 1878, the liver was found affected with fatty infiltration throughout its whole extent, as already mentioned, the above view is sustained by those cases which I observed in previous epidemics, and in which portions of this organ were still found in a state of hyperæmia, preceding that of fatty infiltration or degeneratio

But, while the process of fatty infiltration of the liver is found to have taken place in all fatal cases, and thus forms a typical character of the disease, certain traces of other pathological processes are also discovered to have occurred in this organ in a number of instances, indicating probably a severer form, or other complications of the disease. In the following description of the changes in the parenchyma of the liver, I shall, therefore, begin with that particular condition, observed in the majority of cases; and representing the general type.

When, in these cases, a thin section of the fresh organ is made and examined in water under the microscope, the hepatic cells appear almost completely hidden by larger or smaller fat-globules, and to such an extent as to render the application of ether to the preparation necessary, in order to get a fair view of its component anatomical elements. After the section is cleared up by the ether dissolving the free fat, the hepatic cells will be found more or less distended by a considerable number of fat-globules. The size and quantity of these globules differ in different cells, for while some of the latter may be distended by one very large globule occupying almost the whole interior of the cell, and surrounded by a thin layer of its protoplasm, others may, besides a

few larger globules, also contain a more considerable number of smaller ones. The nucleus is in most cells hidden by the fat. If one of the terminal branches of the hepatic veins—intra-lobular—should be contained in the section or fragment under examination, it will frequently be found that the cells in its immediate vicinity present more or less a greenish-brown color, apparently owing to the presence of bile-pigment. Thus far, the examination of the fresh specimen reveals but little beyond the condition of the hepatic cells, and is, therefore, rather unsatisfactory. But when a very thin section of the same liver is made, after having been hardened in a solution of bi-chromate of potassa, or in Mueller's fluid, and sufficiently large for the purpose, a more perfect view, not only of the individual, but also of the relative condition of all the anatomical elements of the whole parenchyma is obtained when examined under the microscope.

In such sections (Figs. 1 and 2) it will be found, as already mentioned, that generally the cells filling up the neighboring capillary meshes of the hepatic venous radicles, present a more or less dark, greenish-brown color, in some cases mixed with a yellowish tint. The same observation is also made, in a number of instances, on the columns of cells bordering on the radicles of the portal vein (inter-lobular.) These colored cells likewise contain fat-globules, though not as large and as numerous as the uncolored rest, showing that the presence of bile-pigment interfered not with their power of absorbing the fat. The nutmeg appearance of the liver, which was observed in a limited number of cases, as mentioned before—and in which on the contrary the inter-lobular veins were found empty of blood—was probably owing to the coloration of these cells surrounding the vessels.

It is asserted by most pathologists that in the process of fatty infiltration there is no fat deposited outside of the hepatic cells, and that the free fat-globules observed are derived from those cells, cut or torn by the knife in the making of the section. This may be true in cases of phthisis and other chronic exhausting diseases, in which the process of fatty infiltration of the liver is slowly progressing, and sufficient time is afforded to the cells to absorb the fat deposited from the blood into the parenchyma of the organ. In yellow fever, however, where this process fre-

quently arrives at its highest degree in a comparatively short time, and where at the same time—as is true in many cases—the protoplasm of the cells itself degenerates, rendering these minute organs incapable of absorbing the whole of the fat deposited from the blood, it is not at all improbable that a portion of this substance becomes lodged in the interstices of the parenchyma. On the contrary, I may now safely assert that this is a fact, for my careful examination of a large number of well-made and prepared thin sections have not only convinced me of the presence of free fat in the interstices of the parenchyma, but also in those of the connective tissue of the capsule surrounding the organ, and that of the portal vessels (Glisson), or between the latter and the neighboring cells of the hepatic lobules.

In some of the yellow fever livers, the outlines of the hepatic cells appear in the microscopical sections less distinct than in sections made from livers affected with fatty infiltration accompanying other diseases. In the latter, when stained and mounted in Canada balsam, the cells and their nuclei, having absorbed sufficient coloring material, appear very distinct in contrast to the large fat globules which they contain. The hepatic cells of yellow fever livers, on the contrary, do not perfectly absorb the carmine or other coloring materials, in consequence of which their outlines and nuclei appear—especially when mounted in Canada balsam—rather indistinct, and the fat globules within do not show in strong relief. Besides this, in some places of the section, the cells, being filled with numerous minute fat globules, have entirely lost their absorptive power, and, therefore, remain colorless. A great number of the nuclei also undergo fatty degeneration.

The condition of the blood vessels and bile ducts of the liver can be most advantageously studied in these thin sections. Contrary to what might be expected from the observations of some of the clinical phenomena of yellow fever, or from the occasional meeting by way of autopsy with a liver presenting the so-called nutmeg appearance, the blood vessels are, in many cases, found empty of blood. The capillaries, of which, in very thin sections, a number of meshes are frequently met with empty of cells, present here and there a finely wrinkled appearance, which is, however,

owing to minute longitudinal rugae, artificially produced by the action of the hardening fluid, as well as to their complete emptiness; a fine double contour indicates the wall of the vessel, beset by the numerous nuclei, also of normal appearance. I have not succeeded positively in detecting fatty degeneration in the latter, though, in some instances, they presented a fatty luster. The intralobular veins (radicles of the hepatic) were always found empty, and their walls in a normal condition. As regards the coats of the interlobular veins (radicles of the portal), and the interlobular hepatic ducts, they were found in the same condition; only in a number of cases the lumen of the interlobular veins, and of the finer branches of the artery, were filled with blood corpuscles (Fig. 2).

With all the attention which I particularly directed to this subject, *I failed to discover any product of inflammation, either in the form of a multiplication of nuclei, or of a cellular exudate, or, even, of pus;* accordingly, *the theory of an inflammatory condition of the liver in yellow fever, which has formerly been held, and still is, by a number of physicians, proves to be fallacious.*

As regards the multiplication of nuclei in the connective tissue of the capsule of the portal canals, mistakes may easily be made by the unexperienced observer in the examination of preparations which have previously been hardened in a solution of chromic acid or its salts, as this agent alters the colored blood corpuscles in the radicles of the interlobular veins and their capillaries in such a manner as to resemble small slightly refractive nuclei.

To the condition of the epithelium of the hepatic ducts, also, I directed my special attention, expecting to find perhaps a fatty degeneration of the cells, but though in some of the smaller ducts these elements seemed to present a fatty luster, I would not venture to positively assert it as a fact, as in the other instances they appeared perfectly distinct and normal, and, if cut horizontally, the ducts mostly showed an open lumen. In thin horizontal sections of the larger portal canals, the condition of the larger vessels and ducts, and also of that system of minute simple and racemose (hepatic) glands, connected with and opening into the latter, can be studied with advantage. In examining a number of these sections, I failed to detect anything abnormal, either in

the vessels, ducts, or glands; the pathological changes were entirely confined to the anatomical elements of the parenchyma.

Although the process of fatty infiltration extends in most cases throughout the whole hepatic lobule, there are nevertheless certain portions of the latter more affected than others. Thus, it generally appears that the hepatic cells in the immediate vicinity of the intralobular vein are not affected in as high a degree as those of that region of the lobule, situated between the central and peripheral portions, or even the cells bordering on the interlobular veins (Fig. 1.) In thin colored sections, the degree of the infiltration is easily determined by the degree in which the different parts of the lobule are colored. The best colored portion is usually the central, though there are many exceptions to this rule. As mentioned before, there are certain places met with in very thin sections, in which quite a number of capillary meshes are observed almost entirely deprived of their cells. As in the vicinity of such places the hepatic cells are usually very faintly colored, or not all, it appears as if the falling out of the cells from their meshes depended on a degeneration of their protoplasm; besides, uncolored cells ordinarily contain no large fat globules, but are filled with small ones. In such places of the lobule, where the fatty infiltration has taken place in a high degree, a number of the cells present the so-called seal-ring form (Fig. 1), distended by only one large fat globule, while others may contain two or three.

When examining the first yellow fever livers, at the beginning of the epidemic of 1878, my attention was attracted by a singular appearance of the hepatic cells, resembling a division of the protoplasm of these organs into a number of parts, indicated by shady lines. I have since observed it in many instances, and it really appears as if the granular protoplasm of the whole cell were composed of groups of granules, a supposition rendered very probable by the same observation on hepatic cells undergoing fatty degeneration, in which the same grouping of the minute fat globules is observed. However, this is not the only instance in which I observed this phenomenon, for, a number of years ago, I mentioned the fact that the granular substance in the gray matter of the cerebro-spinal axis consists of an aggregation of minute

groups of granules. Even upon the protoplasm of a number of colorless blood corpuscles of man, I have frequently observed this arrangement of the granules.

The pathological changes in the parenchyma of the liver above described are such as I have observed them in the great majority of those cases of yellow fever which I microscopically examined, and from all I know, they may be regarded as typical. In a limited number of cases, however, I observed some additional changes, which either were owing to a severer form of the disease, or to previously existing affections. Thus, I met with two cases in which the coloring of the columns of cells surrounding the intralobular,—or, in some instances, also those surrounding the interlobular veins,—was of a much darker, almost blackish brown, color than in the above cases. Besides, the colored portions or patches were not only confined to the vicinity of the vessels, but moreover met with in other portions of the lobule; in one case, some of these patches presented even a reddish brown. In all other respects, the parenchyma had undergone the same typical changes as above described.

As in all these cases the color was of a greenish or blackish brown, I presume that it depended upon the presence of bile-pigment, though in those few instances where the patch presented the reddish tint, the latter may have depended on the presence of free hæmoglobin, such as was observed in the following case. Here, namely, the patches were of such a size as to be very easily distinguished by the naked eye, and were confined to the intra-lobular veins, embracing them in their entire length (Fig. 3); they were also sharply defined from the rest of the parenchyma of the lobule. Their color was of a dark golden brown, resembling that of old apoplectic foyers in the cortex cerebri. The capillaries of the discolored portions of the hepatic lobules appeared to be compressed, only small portions of them could be recognized with difficulty. The columns of the cells appeared to have been rendered mis-shapen. In each patch, according to the direction of the section of the lobule, a transverse or longitudinal section of an intra-lobular vein could regularly be seen. Though no blood corpuscles could be discovered in the capillaries, there remains no doubt that the coloration of these portions of the

hepatic parenchyma was caused by an extravasation of free hæmoglobin, derived from the colored blood corpuscles, through the walls of the vessels, and finally absorbed by the hepatic cells. Small extravasations of free hæmoglobin are observed here and there in sections of other yellow fever livers, and, as I shall show hereafter, also in other organs; but it is not probable that they often occur to such an extent as in the case last described. Nevertheless, at the commencement of September, 1879, I performed an autopsy upon a fatal case of yellow fever at the Charity Hospital, in which the pathological changes in the parenchyma of the liver were of a much graver character than I had met with before in this disease. The patient, a male, died at 9 o'clock A. M., having vomited a quantity of genuine black vomit three hours before his death; the autopsy was commenced two and a-half hours afterwards. The clinical history of this case, together with the characteristic pathological changes in the kidneys and other organs, as revealed by the microscopical examination, left no doubt about the true character of the disease.

The liver in this case was found rather below the ordinary size, and presented a peculiar aspect. The change of color of the surface—depending on the presence or absence of blood in the intra-lobular and inter-lobular blood-vessels, or on the presence of fat in the hepatic cells—instead of presenting to the eye a uniformity of character over the whole organ, differed considerably in different parts. A considerable portion of the upper surface of the right lobe had a bluish color, similar to that of an ordinarily congested liver, such as is frequently observed in malarial disease, while in other portions the congestion seemed to be confined to the finest inter-lobular radicles of the portal vein. In these portions, also, the parenchyma showed the pale yellowish tint, though not so distinctly as is usually seen in this disease. By a closer inspection, however, numerous portions in the form of larger and smaller well-defined patches, ranging in size from that of a hepatic lobule to a ten-cent silver coin, or even larger, of a decided yellow color and without traces of congestion, were discovered, especially upon the upper surface. And, furthermore, in the bluish congested portion of the right lobe, dark, bluish or reddish-brown patches, irregular in size and form, and

having the appearance of extravasation of blood, were also noticed. A section through one of the patches showed that they extended in an irregular form into the substance of the organ to the extent of about one inch or more. The consistency of this liver was rather below the normal. A microscopical examination of the fresh parenchyma from the vicinity of the dark patches showed the simultaneous existence of atrophy and fatty degeneration of the protoplasm of the hepatic cells, together with a slight fatty infiltration, consisting of large fat globules.

After portions of the organ had been sufficiently hardened in Mueller's fluid, thin sections were made of different portions of the organ, and colored with carmine, the examination of which disclosed the extraordinary changes, to be now described, which had taken place in the parenchyma of this liver.

To get a correct idea of the whole pathological process which had been going on in this liver, would require a minute description of every detail, with a discussion too extensive for our present purpose. Therefore, a brief sketch of the condition in which the parenchyma was found must suffice. At the first glance through the microscope, upon a section through one of the dark bluish patches and made vertically to the surface of the organ, the anatomical elements of all the hepatic lobules contained in the section appeared to be in a chaos and confusion ; for in some places round patches, colored by carmine, were noticed, while in others certain curved columns of cells of a lighter or darker brown, or others uncolored, were also observed. In many places between these portions the cells had disappeared, and through the empty spaces they had left, the field of the microscope could be discovered. The whole parenchyma bordering the inner surface of the general capsule of the upper surface of the liver, contained in the preparation, was, to a considerable depth, found to have assumed a brown color, deepening in shade almost to black, in proportion to the thickness of the section. By repeated examinations with lower and higher powers of a considerable number of sections, I was enabled to study the condition of their individual elements and parts throughout, and, thus far, arrived at the following conclusion. Accordingly, the pathological changes observed in this case, must have been preceded by a hyperæmic

condition of the utmost intensity, not only of all the branches of the portal vein, but also, as the examination shows distinctly, of the capillaries of the peripheral portions of the lobules. The intensity of this hyperæmia was such as to induce the hæmoglobin to leave the blood corpuscles, and pass through the walls of the vessels into and between the neighboring cells, a phenomenon which is usually observed in association with a stasis of blood in the vessels. But, besides this extravasation of the coloring material of the blood, a rupture of some of the capillaries must also have occurred, as, in many places, great numbers of blood corpuscles were found located between the atrophied cells. During this state of congestion of the portal veins, the circulation of the blood through the remaining portion of the parenchyma appears to have been mainly carried on by the branches of the hepatic artery, particularly by those arising in the substance of the liver, and passing to the general capsule—rami capsulares arteriosi—which, after extensively anastomosing with each other, give rise to other branches returning into the substance of the organ, and terminate in the capillaries of that portion of the parenchyma situated beneath the capsule. In the sections, these vessels are well displayed, and, as it appears, enlarged in their caliber. As a consequence of the pressure produced by the congested portal veins and their capillaries, and, furthermore, of the simultaneous diminution of the nutrition of the hepatic cells, atrophy of the protoplasm of the latter occurred, not only of those of the peripheral portion of the lobule, but also of those of the center, surrounding the terminal branches of the hepatic veins. Thus, in examining the central portion left in a number of lobules, it appeared as if these cells consisted entirely of nuclei, each surrounded by only a very thin layer of protoplasm. Notwithstanding this atrophied condition of the hepatic cells, however, the whole mass appeared perfectly colored by the carmine, showing that fatty degeneration had, as yet, not taken place in this portion of the lobule. In most of the lobular centers a transverse, or also a more or less longitudinal section of an intra-lobular vein was seen, the lumen of which, in most cases, was filled with a fibrinous thrombus; the walls of these vessels were thickened and contained numerous small spindled-formed cells. In directing my attention to the peripheral portions of the

lobules, I could distinctly recognize the form of the capillary meshes, which presented a lighter or darker brown color, the same as is generally observed on blood vessels distended with blood after having remained for some time in a solution of chromate of potassa and subsequently colored with carmine. But the diameter of the capillaries forming these meshes appeared much increased, owing to being still surrounded by a layer of hepatic cells, though the center of the mesh was more or less empty. With an adequate amplification, the blood corpuscles in the interior of these vessels could be well discerned, together with those which had escaped into the surrounding cells, colored brown by the hæmoglobin escaped from these vessels. But there were also here and there empty meshes met with, of which the atrophied cells surrounding the capillaries were colored only by the carmine, showing that they had not absorbed hæmoglobin, nor undergone fatty degeneration. In other places, similar curved columns of cells were observed, which, lying parallel with the periphery of the lobule, and, separated by empty spaces, appeared in the form of successive strata. It would be difficult to describe the details of the destructive process by which these appearances of the parenchyma were produced, though it is obvious that the empty spaces were formed by the degeneration and breaking down of the hepatic cells of this portion of the lobule Many of these columns, also, were uncolored, their cells having undergone fatty degeneration. Finally, in some places, every trace of an arrangement into lobules appeared to be obliterated, the remaining elements representing a confused mass of degenerated cells, broken here and there by an empty space, or by an isolated section of an intra-lobular vein. Sections of portal vessels were also observed, but their structure appeared indistinct and thickened. The greater number of these represented inter-lobular branches of the hepatic artery, highly colored with carmine. Sometimes, long columns of carmine-colored, though atrophied, cells were encountered, which, as I suppose, consisted of an arterial branch, surrounded by a layer of cells having, perhaps, received their nourishment from this vessel, preventing their degeneration.

From the above it will be seen that the relative pathological

condition in which the anatomical elements of the lobules of the atrophied portions of this liver were found, does not exactly correspond with the condition of the same elements observed in the so-called yellow atrophy of this organ. In the fatty degeneration met with in both instances, as well as in some other minor points, however, a certain resemblance evidently exists. The view, entertained by *Rindfleisch*, that yellow atrophy depended upon an infectious poison, may be true in the case above described.

As regards the other less congested portions of this liver, which formed the greater part of the organ, they were found in the same condition as has been described as "typical" of yellow fever. However, the fatty metamorphosis, observed in this case, was a true fatty degeneration of the hepatic cells; all other elements, as capillary and other vessels, etc., were in a perfectly normal condition; in some form of these capillaries blood corpuscles were observed. There was no atrophy of the cells, they had retained their normal size, but were filled with minute fat globules, which exhibited very distinctly the arrangement in minute groups of which I have spoken above. Only in a comparatively small number of these cells, two or three larger fat globules—though not very large—were observed.

In connection with the pathological changes met in the parenchyma of this liver, I cannot forbear to mention a singular discovery which I made in sections made from those dark bluish portions, and relating to the presence of the mycelium of a very minute parasitic fungus, which extended its numerous filaments throughout the parenchyma of this particular portion of the liver. Not being, myself, an enthusiastic supporter of the so-called germ theory, I would have passed this observation without mention, if the circumstances connected with the presence of this fungus in such an unusual place, would clearly show that the minute plant found its way into the liver accidentally after death. But this is not the case, as the chances for such an accident were quite limited. The autopsy was made two and a half hours after death. The liver, being one of the first organs removed from the body, was put into a basin, and covered with large pieces of ice. There it remained about two hours, when certain parts of it were cut out, and, after being cut again into small cubes of about one

to one and a quarter inch diameter, were put, together with pieces of kidney and other organs, into a sufficient quantity of Mueller's liquid. On the second day after, the fluid was removed, and the same precaution was twice more taken before the pieces were hardened enough to be transferred into a fifty per cent. mixture of alcohol and water. A few days after the pieces had been put in Mueller's liquid, I examined some small sections made by hand from one of the pieces belonging to that dark bluish portion of the liver above described, and observed, especially at the thin edges of the section, the fungus consisting of a mature spore with two germinating filaments arising from it at opposite poles. Each filament was bordered by a fine double contour and its interior filled up by a distinct row of granules. At the first sight of these elements, I must confess that I knew not what to make of them, until I met with a bifurcating filament, and observing, furthermore, a peculiar luster on some of the granules in the interior, I began to suspect them to be of a fungous nature. Though these elements might be confounded with long spindle-form cells, a closer examination would easily show a difference existing in the details of both. When the pieces were sufficiently hardened, I was enabled to study the further details of this fungus on the thin sections made by the aid of the microtome. From these examinations, I found that it belonged to one of those families the most simple in construction. The elements which I first observed along the edges of the section, or floating about, represented germinating spores, each of which had given origin to two or three filaments of about four, five, or six times the length of the former. A sporangium was formed upon the terminal points of these filaments, containing about two or three sporules, the discharge of which I witnessed in a number of instances, as also the detachment of the sporangium from the filament. In many specimens, the filaments presented a number of varicosities in their course, sometimes only on one side, almost resembling suckers; in some of them the base was much thicker than the point, and filled with granular protoplasm which had entered from the mother spore; I have also seen the disintegration of the latter. In other instances, again, I observed secondary filaments arising from the first; and likewise bearing a sporangium, or even com-

municating with a filament of a mother spore. Not being sufficiently versed in systematic mycology, I have failed to classify this fungus, though I have consulted some standard works on the subject. Judging from its mode of fructification, however, it seems to resemble more the Peronospores than any other family.

The presence of this fungus in the parenchyma of this liver, of course, cannot be regarded as an unusual phenomenon, for it might be supposed that it was primarily contained in the hardening fluid, whence it made its way into the pieces of liver. But, then, it would most likely also have invaded all other pieces, not only of the same liver, but also of the other organs contained in the same jar. This, however, was not the case, for, with the exception of the dark bluish atrophied portions infected by the fungus, no trace of the latter could be discovered in those pieces of the same liver affected only by fatty degeneration, or in the pieces belonging to other organs. The only explanation, therefore, left to account for the presence of the fungus in the place mentioned, is, that it was primarily contained in the Mueller's fluid—though this was freshly prepared—and that it selected particularly these disorganized atrophied portions of liver as the best nidus for its development. Whether it was possible that the fungus, or its spores, penetrated by some way or other into the portal circulation, and finally became lodged in some of the interlobular veins, giving rise to the intense congestion and ensuing atrophy of the parts above described, I must leave to the germ theorists to decide. At any rate, I regard the observation sufficiently interesting to be worthy of report, although I entertain not the slightest idea of its standing in any relation with the pathology of yellow fever.

The pathological changes in the parenchyma of the liver, characteristic of yellow fever, as described in the preceding pages, are equally observed in cases where this disease supervened upon another, accompanied by organic changes in the tissues of the same organ, a coincidence which may specially occur in cases of cirrhosis of the liver. An illustrative case of this kind, sufficiently interesting to be cited, I had an opportunity to observe and to examine after death during the epidemic of 1878. A young man of small stature and delicate build, an Italian, was

admitted to one of the wards of the Charity Hospital. As I was present at the time, I had occasion to examine him myself. Finding him in an unusual state of nervous exhaustion—for he could hardly walk—with an intensely jaundiced skin, and a very feeble pulse, but otherwise—as could also be gathered from his history—no symptoms of yellow fever about him, I regarded the case as one of chronic malarial fever. As he could speak neither English nor French, himself, it was ascertained by an interpreter that he had been sick for two months, and had been staying with the "Spanish Colony,"—as a portion of the Spanish and Italian population of New Orleans, who, during the epidemic, had left the city to encamp several miles above near the bank of the Mississippi, was called,—whence he came to the hospital. Though at one time slightly improving from his nervous exhaustion, this patient eventually contracted the yellow fever in the hospital, from which he died. The autopsy revealed the following condition of the organs. Not only the skin, but all other tissues in the interior of the body were intensely yellow throughout. The lungs, with the exception of some old slight adhesions to the walls of the thorax, presented a healthy appearance. The heart, also, appeared normal, though the fluid contained in the pericardium was yellow. The liver was enlarged, hard, and granular, showing its cirrhosed condition by gritting under the knife when cut; its capsule was thickened, and its vessels and bile ducts were congested, bile issuing from the cut ends of the latter. The walls of the gall bladder were œdematous. As the patient had thrown up black vomit not long before he died, the stomach was found empty, though its mucous membrane presented that condition of congestion peculiar to yellow fever. The spleen was greatly enlarged, five or six times the bulk of a normal spleen, and also gritted under the knife when cut. The pulp was of a dark color, while the trabeculæ appeared white and enlarged; the capsule of the organ was thickened. The peritoneum covering the diaphragm, liver, stomach, spleen, pancreas and transverse colon, was much thickened, having glued these organs to each other, thus showing that a chronic peritonitis had been existing. The kidneys were greatly enlarged and much congested. The veins of the intestines were filled with blood, though otherwise these

organs had a normal appearance. In the cranial cavity the dura mater was yellow, but otherwise healthy, though the vessels of the pia mater were much congested; the arachnoid membrane was found opaque in some places. The cerebral and basilar arteries with their branches were filled with blood. The substance of the brain appeared œdematous, and the ventricles were filled with a yellow fluid. The corpora striata appeared rather pale, while the thalami optici were very white; the superficial vessels of these bodies were filled with blood. In a section of the cerebral hemispheres, the medullary substance appeared very white, the cortical layer pale gray.

The microscopical examination of thin sections of the liver showed that the cirrhosis in this case existed in a considerably high degree. The capsule of Glisson, undergoing the usual hyperplastic metamorphosis, represented now a connective tissue of a coarser and stiffer appearance, than when in its normal condition, though no proliferation of nuclei or spindle cells could any more be observed. The cicatricial tissue formed had encroached upon the lobules, and, in many places, extended into their interior, separating portions of them, which, in the section, appeared in the form of small islands. The hepatic cells at the periphery of the lobules presented a greenish brown color, while minute masses of black pigment were here and there observed deposited between the hepatic cells. The central portions of the lobules, or, also, the portions intermediate between these and the peripheral, were invariably found affected with fatty infiltration (Fig. 4.) This condition existed in a considerably high degree, for most of the cells of the affected portions presented the seal-ring form. In the newly formed tissue of the capsule of the portal vessels the remains of blood vessels were also observed.

Very frequently, especially in cases of drunkards, cirrhosis of the liver is found associated with fatty infiltration. In these cases, however, as in those of ordinary fatty infiltration without cirrhosis, the infiltratory process almost always commences in the hepatic cells at the periphery of the lobule, while in yellow fever, as we have seen, the process appears to commence, or to attain at least its highest degree, near the center, or in portions of the lobule situated intermediate between the latter and the periphery.

THE STOMACH.

In all serious cases of yellow fever, whether terminating favorably or not, this organ, like the liver, is deeply involved in the pathological process, originally called forth by the introduction of the specific poison of the disease into the blood. In consequence, the clinical symptoms arising from this implication of the stomach, and consisting mainly in a disturbance of its circulation, are, as we have seen, very annoying to the physician, and, at the same time, so distressing to the patient, as to have induced a number of the older physicians and authors to even regard this organ as the true seat of the whole disease. Although it may be justly presumed that the functional disturbances of the stomach are partly depending on the common cause—the presence of the poison in the blood—it is nevertheless true, that the congestion of the gastric veins is only secondary in its nature, depending upon the imperfect portal circulation in the liver. The condition of the stomach, therefore, may in all cases, as I have before hinted at, serve as a true index to that of the liver. And, in order to render the demonstration of the disturbances in the gastric circulation more perspicuous, it may be proper to briefly review the particular blood vessels supplying the mucous membrane of the stomach with blood, and their arrangement

It will be remembered that the larger blood vessels sent to the stomach form two arches along the so-called curvatures of this organ. The arterial arch along the lesser curvature is formed by the union of the *coronary* artery and of the *pyloric* branch of the hepatic, while that along the greater curvature is formed by the right *gastro-epiploic* branch of the splenic artery; the latter, also, furnishes some small branches, the *vasa brevia*, to the "cul de sac." The veins, corresponding to these arteries, return their blood to the splenic and superior mesenteric veins, which by their junction form the portal vein; sometimes the coronary vein joins the latter directly. The branches arising from these vessels, both arteries and veins, in entering the walls of the stomach, penetrate through its muscular coat to be distributed throughout the sub-mucous tissue in which they divide into subordinate branches. Of these, the finest arterial branches

penetrate the muscular layer of the mucous membrane, and arriving at the glandular layer, give rise to a network of capillary vessels with oblong meshes surrounding the individual gastric glands, and extending to the vicinity of their apertures. Here the capillaries of the network somewhat enlarge in diameter, while their meshes assume a more regular polygonal form, each mesh surrounding the aperture of a gland. From these larger capillaries the venous radicles take their origin in the form of minute branches, a small number of which, representing a small district of the mucous membrane, join to form a somewhat larger vessel, which, without receiving any additional branches, descends vertically to join a venous network, extending between the glandular and muscular layers of the mucous membrane. From this network, other branches arise, which, by penetrating the muscular layer, join those larger veins ramifying, in company with the arteries, throughout the sub-mucous tissue, and which finally penetrate the other coats of the stomach to reach their ultimate destination, the splenic, or superior mesenteric vein.

As regards the function of the capillaries of the mucous membrane of the stomach, it may be mentioned that the larger kind, forming polygonal meshes around the apertures of the gastric glands, have been regarded as subserving the process of absorption, while those surrounding the gastric glands themselves, smaller in diameter, and forming oblong meshes, are considered to furnish the material for the secretion (*Frey*). We may now proceed with the description of the pathological changes taking place in the mucous membrane of this organ.

In almost all cases of yellow fever, this membrane is found more or less congested. The congestion, however, does not extend uniformly throughout the whole membrane, or even larger portions of it, but is confined to smaller or larger spots or districts, in which it is observed to proceed from one or more centers. From these centers it extends or radiates in a lesser degree, either gradually to be lost, or to pass over to another congested district. It is owing to this peculiarity of the congestion that it presents no uniformity of character, but is observed to spread irregularly over larger or smaller portions of the membrane. Neither are the congested portions of the latter limited

to any particular region of the organ; they may be nearer to the cardiac, or to the pyloric extremity; in most instances, however, they are found in that portion forming the greater curvature. In examining the congested portions of the mucous membrane with a loupe, magnifying about five diameters, the congestion will be found confined to the minute venules, presenting an arborescent arrangement resembling the broken meshes of a vascular network (Fig. 6, *a*). From the center of each individual district, corresponding to the apparent trunk of these minute vessels, a few fine branches are seen to proceed, which in their turn give rise to still finer ones, the whole resembling the branch of a tree without leaves. From our description of the arrangement of the blood vessels of the mucous membrane of the stomach, given above, it may be inferred that the finest of these vessels are identical with those minute venules arising in the upper and larger capillaries, surrounding the apertures of the gastric glands, and that the branches, formed by their junction, converge to a common center, in order to form one of those larger vessels, which, without receiving any additional branches, descend betwen the gastric glands (Fig. 5) to join their respective venous network extending between the glandular and muscular layer of the mucous membrane.

This particular form of congestion prevails in a greater or lesser degree in almost all the congested portions of the membrane. Each descending venule or vein, as has been seen, forms one of the centers, while its minute tributaries represent the districts. Nevertheless, in most fatal cases, besides this particular form of congestion, a number of small and defined spots or patches are also found, presenting a distinct red color, and resembling small ecchymoses or extravasations of blood. Their size is very limited, ranging from that of a mere dot to about two or three mm., seldom more; and if they are examined with a strong loupe, they are found to consist of an unbroken network of minute vessels, congested with blood (Fig. 6, *b*), and identical with that network of large capillaries which surrounds the apertures of the gastric glands. In most instances, these small congested spots or patches are found between or along the sides of the plicæ, sometimes extending over the summit.

In examining thin sections made vertically through one of these small congested patches, the peculiar character of the congestion can be clearly demonstrated. In such sections (Fig. 5), then, it will be found that, wh·le the arteries with their *capillaries*, surrounding the gastric glands throughout nearly their entire length, are *empty*, all the veins throughout the entire wall of the congested portion of the stomach are congested with blood. The congestion commences in the network of large capillaries, surrounding the apertures of the glands, whence it extends through the venous radicles to all other veins of the organ, contained in the section. These large capillaries, especially, are distended with blood corpuscles, which, in a number of places, may be observed to have ruptured the minute vessels, and extravasated into the surrounding tissue. In other places, again, no rupture has taken place, but, in consequence of the stasis of blood, which obviously must have existed in these localities, the blood corpuscles have parted with their hæmoglobin, which, passing through the walls of the vessels, was absorbed by the neighboring epithelial cells, as shown by the brown color they present to the eye of the observer. Thin sections, sliced off with a sharp knife from the surface of one of these spots, embracing the outer epithelium, also show distinctly the condition of the membrane just described. It will be easily understood that the hæmorrhagic effusions into the stomach, occurring during the course of yellow fever, and represented by the "black vomit," are derived from the rupture of these minute vessels. In the numerous sections of the mucous membrane of the stomach which I have examined, I have failed to discover any product of inflammation.

It has been asserted, and is believed by a number of physicians, that in yellow fever the epithelium of the stomach underwent fatty degeneration. During the epidemic of 1867, but particularly during that of 1878, I had carefully examined the fresh epithelium of a considerable number of stomachs without finding any traces of this degenerative process. Nor can it be demonstrated in the thin sections of the hardened specimen, in which the details of the cellular elements can be minutely studied. On the contrary, it is not only found that the epithelial and

glandular cells contain no fat globules, but, moreover, that their protoplasm is very readily colored by the staining liquid.

With the exception of the pathological changes above described, none are observed in the remaining tissues of the stomach.

THE INTESTINES.

The distribution and arrangement of the blood-vessels of these organs being very nearly the same as that met with in the stomach, it may be expected that the congestion of these parts also partakes of the same character. But though, in the greatest number of fatal cases, the larger veins, emerging from the walls of the intestines to become tributaries of the portal vein, are found filled with blood, the congestion of the minute vessels of the mucous membrane very rarely attains as high a degree as in the same membrane of the stomach. An explanation of this fact may be found in the distance intervening between the portal vein and the mucous membrane of the intestines, being greater than that existing between this vessel and the mucous membrane of the stomach. The first effect of any retardation of the portal circulation of the liver will, of course, be felt in those tributaries which the portal vein receives nearest to this organ. For this reason, hæmorrhages into the intestines only take place in very severe cases, though a congestion of the venous radicles is frequently observed, especially in the upper portion of the small intestines. When blood is observed to pass from the bowels, however, it does not always signify that a hæmorrhage from the mucous membrane of the intestines has occurred, as it may possibly be derived from a hæmorrhage into the stomach, and, instead of being vomited, be discharged by way of these organs. The appearance which the congested mucous membrane of the intestines presents to the eye of the observer is very similar to that of the congested portions of the stomach above described, having its seat in the minute venous radicles. Those small red spots or patches, formed by a congestion of the larger capillaries, surrounding the apertures of the glands, are rarely met with upon the mucous membrane of the intestines.

THE SPLEEN.

This organ is almost always found in a normal condition; any deviation from the latter should, as in the case of the lungs, be considered as having no relation with yellow fever, but depending upon other causes. The only pathological phenomenon which the microscopical examination in some cases reveals, consists in the presence of small masses of black pigment, deposited in the pulp of this organ, but which are frequently met with in malarial spleens and livers. The blood-corpuscles, neither, present anything remarkable in their form, or otherwise. These statements are based upon the examination of the fresh pulp in a number of cases, and, furthermore, upon that of thin microscopical sections of the hardened specimen.

THE KIDNEYS.

In almost all fatal cases of yellow fever, the microscopical examination shows that certain pathological changes have taken place in the parenchyma of these organs. These changes, as I shall show directly, chiefly consist in a degeneration of the epithelium lining the uriniferous tubules, and, in some instances, they exist to so small an extent as not to alter the normal appearances presented by the cut surfaces of the kidneys to the naked eye. Among the autopsies which I performed during the epidemic of 1878, I met with a number of such specimens of kidney, the normal appearance of which so much misled me as to make me indifferent to their preservation. Subsequent microscopical examinations of thin sections made from similar specimens, however, showed me that even in these kidneys of normal appearance the peculiar changes do exist, and are easily demonstrated; and, in consideration of their almost constant occurrence, they may safely be regarded as characteristic of yellow fever.

As the anatomical construction of the kidneys is quite complicated, I do not consider it out of place to briefly review it before proceeding to the description and discussion of the pathological phenomena observed in these organs.

When a kidney is divided longitudinally, the cut surface appears as if consisting of two different substances. The one forming the external portion of the organ, and accordingly called "cortical," presents a granular appearance, while the other, called "medullary," is collected in conical or pyramidal masses, and appears to consist of bundles of fibers, converging in each pyramid from the base to the apex. Thus the kidney may be regarded as composed of the cortical substance and about a dozen, or more, of these conical bodies, the bases of which are connected and surrounded by the former, while their apices, represented by the *renal papillæ*, project into the cavity, or *sinus*, of the organ; and, furthermore, each pyramid, together with its respective portion of cortical substance, may be looked upon as a separate gland. In embryonic life, the kidney really consists of a number of minor kidneys, held together by connective tissue, which subsequently become blended with each other. The secreting portion of the kidney is represented by an immense number of tubules, lined by a layer of epithelial cells, the true secreting elements. The mutual relationship of these tubules is quite simple, consisting in the junction which a number of the primary tubules form with a particular kind of straight or collecting tubules, and in the union of these to form, finally, still larger ones, the *ductus papillares;* but the changes which they undergo in their diameter and in the direction of their course, together with the peculiar arrangement and distribution of the blood-vessels, render the study of the renal parenchyma rather complicated. The apparent difference existing between the cortical and medullary substances is owing to these variations existing in the diameter, form, and course of the uriniferous tubules, and in the arrangement of their minute blood-vessels, though a distinction may be presumed to exist in their functions: that is, the cortical substance representing the proper secreting portion of the gland, while the medullary, consisting entirely of straight and larger tubules, represents that portion through which the secretion is discharged.

If the cut surface of the cortical substance is examined with a sufficiently strong loupe, a considerable number of minute spherical bodies will be observed; these are the so-called "Malpighian

bodies," upon which the uriniferous tubules commence. Each of these bodies consists of a conglomeration of minute vessels, surrounded by a thin capsule, the continuation of which, in the form of a short and narrow constriction or neck, represents the commencement of a uriniferous tubule. The capsule itself, consists only of a layer of flat pavement cells (endothelium), surrounded by a thin layer of connective tissue, while the tubule, throughout its entire length, represents a tube of a structureless so-called basement-membrane, lined by an epithelial layer of cells, which, in different portions of the tubule, assume a different form and arrangement. The tubule, after having arisen by its neck from the capsule, rapidly enlarges in diameter to form a comparatively wide tube, which, bending into several convolutions, pursues its course in a slightly oblique direction toward the center of the kidney; but, diminishing again in diameter to about one-third of that of the convoluted portion, it suddenly makes a turn and descends vertically toward the medullary substance, forming thus what is called the *descending limb* of the tubule. After penetrating, to a lesser or greater distance, into the medullary substance, it makes, opposite to the side whence it came, a short bend upon itself (loop of *Henle*), and ascends again in a vertical direction, forming the *ascending limb*. Having passed beyond the height of its respective Malpighian body, it again enlarges in diameter, and forms the *intermediate* portion or canal, consisting of a few convolutions. This portion, after being once more reduced in diameter to a very fine tubule, makes a turn sideward to join its respective *collecting* tubule. The collecting tubules commence near the surface of the kidney, where they receive a limited number of primary tubules, and thence pass, without receiving any others, in a direct vertical direction into the medullary substance. Here, in uniting with others of their own kind, they form larger tubules from which, by successive union, the ductus papillares finally result.

The initial or convoluted portion of the uriniferous tubule is lined by an epithelium consisting of cells of a turbid appearance, and of a slightly conical form, resting with their bases upon the interior surface of the basement-membrane of the tube, and presenting their smallest surfaces (the apices) to the lumen of the tube. In

the narrow descending limb, to some distance beyond the loop of Henle, the epithelium consists of smaller cells arranged in the form of a pavement, their nuclei projecting into the interior of the tube. In the ascending limb, the cells assume a somewhat squamous arrangement up to the intermediate canal, which is lined by the same epithelium as found in the convoluted portion of the tubule. The epithelium found in the collecting tubules, and in those larger ones formed by the latter, consists of slightly conical cells, presenting their smallest surfaces to the lumen of the tube.

In the same manner as the kidney is composed of a certain number of conical or pyramidal bodies, these, on their part, consist of a considerable number of primitive cones formed by bundles of collecting tubules, together with the primary tubules they receive. These bundles may be regarded as separate lobules of the gland, for all the collecting tubules of one bundle are received by one and the same of the larger tubules, by which, finally, the ductus papillares are formed. And it is by these separate bundles of collecting tubules that the peculiar striated appearance, observed on the cut surface of the organ, is produced, the striæ being formed by the bundles and their interspaces. In the latter, the blood vessels are lodged.

The distribution of the blood vessels in the kidney is rather peculiar. The smallest branches, resulting from a successive division of the renal artery, proceed at once to the inner border of the cortical substance. Here they give rise to two sets of minute vessels -the *inter-lobular* (arteriæ interlobulares) and the *straight* arteries (arteriæ rectæ), which proceed in opposite directions. The interlobular arteries enter the cortical substance, and, lodged in the interspaces of the primitive cones, pursue their course toward the surface of the kidney, while, at the same time, they send minute arterial twigs (vasa afferentia) to the Malpighian bodies. Each of these arterioles penetrates the capsule of one of the latter, and then divides into a limited number of capillary vessels, which, after having formed a number of loops among themselves, reunite to form again another minute vessel (vasa efferentia), which leaves the capsule near the place at which the afferent vessel had entered. The conglomeration of vessels thus

formed in the interior of the capsule represents the so-called "glomerulus." After having left the glomerulus, the efferent vessel terminates in the true capillary network surrounding the uriniferous tubules of the cortical substance, and giving rise to the radicles of interlobular veins.

The straight arteries, arising by a short trunk from the same renal branch as the interlobular, enter the medullary substance, in which, lodged in the interspaces of the primitive bundles of tubules, they give rise, successively, to small bundles of very fine straight vessels, the subordinate branches of which terminate in the regular capillary network, surrounding the tubules of the medullary substance, and consisting of long meshes. The vasa efferentia of the glomeruli near the border of the cortical substance, also, join this network of capillaries, in which the venous radicles of the straight veins arise.

Before dismissing the anatomical construction of the renal parenchyma, it may be further remarked that the glomerulus has no direct connection with the interior surface of the capsule, being only suspended in the cavity of the latter by its root, formed by the afferent and efferent vessel; neither does the liquid contained in the cavity directly touch the walls of the capillary vessels, they being covered by a layer of delicate cells, the nuclei of which are conspicuously distributed over the entire glomerulus.

While in the parenchyma of the liver the degenerative process, as we have seen, chiefly consists in an infiltration of fatty matters, derived from the blood and absorbed by the hepatic cells, we find it represented in the kidney by a true degeneration of the protoplasm of the epithelial cells lining the uriniferous tubules. The pathological process in the kidney appears to be initiated, as in the liver, by a general hyperæmia of the organ, the traces of which may still be detected by the microscopical examination. But, as in most fatal cases of yellow fever the congestion has, at the time of death, become greatly diminished by the ensuing degeneration, it is not often, when the autopsy is made, that the kidneys present a highly congested condition. Nevertheless, I have met, in former epidemics, with a limited number of cases, in which the kidneys presented the reddish-blue color of congestion to a considerable degree. And even in those kidneys

in which the degenerative changes have already become perceptible to a microscopical examination, some portions of the organ may still be found in a state of hyperæmia. The traces of the congestive stage of the kidneys are best studied in thin sections. The microscopical examination of these sections shows that, in most cases, the congestion was at the time of death confined to the straight and interlobular veins, which are still found filled with blood corpuscles. However, not unfrequently a number of the capillary vessels, especially those along the border of the medullary substance (Grenzschicht of *Ludwig*), forming oblong meshes, are also found filled with blood. And, moreover, in some instances, I have even observed the minute vessels of a number of glomeruli in the same condition, indicating that the congestion must have extended throughout the capillary network of the cortical substance; and, in considering the contraction of the minute arteries, very probably taken place at the time of death, it may be presumed that, even in those cases in which only the minute veins were found filled, the congestion had likewise existed in the capillary network before the fatal issue took place. The presence of hæmoglobin, which in a number of cases may be demonstrated in the epithelium of the uriniferous tubules, moreover, corroborates the latter supposition.

The degenerative process, taking place in the renal parenchyma during the course of yellow fever, is in some respects peculiar, and appears not to resemble, in all points, the fatty degeneration of the kidney observed in connection with parenchymatous nephritis. The chief part of the process rather consists in a gradual breaking down and dissolution of the epithelial cells of an indefinite number of uriniferous tubules, terminating in most instances in a fatty metamorphosis of the remains. As a result of the degeneration, numerous so-called albuminous cylinders, and other infarctions, differing in composition and form, are formed in the interior of a considerable number of uriniferous tubules. These urinary infarctions, met with in certain organic affections of the kidney, have, since their discovery, always attracted the attention of pathologists, and as the probable origin and mode of formation seems to be still an open question, I shall endeavor to render a true account of their appearance in the yellow fever

kidney, and also of their relationship to the degenerated epithelial cells. In doing so, I shall discuss the most prominent points of the question with special reference to their bearing upon the pathology of yellow fever. But, in order to facilitate the description of the condition and probable nature of the degenerated cells, and of the infarctions, I should make some preceding remarks upon the advantages derived from staining the thin sections of kidney with carmine, a valuable accessory in these studies, for the purpose of discriminating correctly between the different degrees of degeneration in which the cells may be affected, and also for determining the particular nature of the different forms of infarctions.

Knowing, namely, that the absorptive power of an organic cell is proportionate to the normal condition of its protoplasm, the extent or degree of the degenerative process, going on in the latter, may be determined by the degree of the coloring. The epithelial cells of the uriniferous tubules, therefore, will be perfectly colored as long as they are in their normal condition, but as soon as their protoplasm commences to degenerate, their absorptive power diminishes, and they appear only faintly colored; or, if the process of degeneration has farther advanced, the protoplasm remains colorless, while the nucleus may still be colored, or, if likewise degenerated, remain uncolored. The fatty matters resulting from the metamorphosis, remain, of course, uncolored, and appear yellowish when seen under the microscope. The so-called albuminous cylinders possess a considerable power of absorption, and appear highly colored. If hæmoglobin is present in the cells, they assume, in proportion to its quantity a more or less brown color; in relation to this body, especially, the carmine is preferable to other colors.

The infarctions formed in the uriniferous tubules during the course of yellow fever, differ somewhat from each other in their origin and formation. A number of them represent albuminous cylinders, while others consist of the remains of degenerated epithelial cells, or may even be composed of both. They are met with in all portions of the uriniferous tubules, and in correspondence with the diameter of these canals, vary in thickness. The largest are found in the convoluted portions, the so-called tubuli

contorti, and in the intermediate canals (Schaltstuecke of *Schweigger-Seidel*), which they frequently fill up throughout their entire length. In the ascending and descending limbs and in the collecting tubules, they only exceptionally attain a great length, being generally short in extent. The relative number in which they are found differs considerably in different kidneys, and is proportionate to the extent of the pathological condition of the organ, which, as has been remarked before, greatly differs in different cases. Neither do the particular forms of infarctions stand in any fixed relation to the extent of the destructive changes in the kidney, for, while a considerable number of the simple albuminous cylinders may be met with in one case in which these changes exist to a great extent, they may hardly be observed in another case, in which only a comparatively small number of uriniferous tubules may be affected by the degeneration, or be obstructed by another form of infarction. In the same way does the degree of the degenerative process not always correspond to the extent in the organ, for there are cases met with in which few, or even no albuminous cylinders are observed, and in which the epithelium of only a small number of uriniferous tubules are found to undergo degeneration, but in which the latter process has nevertheless arrived at the fatty metamorphosis,—while there are other cases again, in which the formation of fat is hardly observed. To explain this discrepancy in the extent or degree of the pathological changes in the yellow fever kidneys, the comparative length of time preceding the fatal issue, and also the severity of the attack, must be considered; for, in those cases of a rapid course, and in which the patient succumbs in a few days from the effects of the cerebral disturbances, the kidneys may be found affected to only a small extent, while in other, more protracted cases, more time is afforded to the pathological process to extend farther throughout the organ.

Before proceeding to the description of the infarctions, a previous examination of the particular condition of the epithelium of the uriniferous tubules, which not only furnishes the material to the greater number of the obstructions, but, moreover is probably otherwise instrumental in their formation, may not be considered out of place. And, for this purpose, I shall refer in my

description to one of those cases, in which the pathological changes observed are decidedly pronounced.

In examining a very thin section of kidney of such a case (Fig. 7), perfectly stained with carmine, it is found that the epithelium in the tubules has considerably diminished in its normal thickness (*b*). This observation is made as well on the entire tubule as on the transverse section of it. In the convoluted portions of the tubules, especially those surfaces of the cells directed toward the lumen, and which in the normal condition are conical, are now observed to be flat, causing the cells to appear rectangular in form. The lumen of such a tubule, as it is seen in a transverse section, therefore, will be found much larger than it is in the normal condition, though the epithelium may be intact; this is owing to the cells having lost their turgescent and conical appearance. In many cells, especially when viewed in profile, the nucleus appears more deeply colored than the protoplasm of the cell, while in others the color is more evenly diffused throughout the whole. In the greater number of tubules, the epithelium appears intact, but there are many others in which it is detached from the basement-membrane, leaving an interspace between it and the latter. In a number of other tubules, portions of the epithelium are observed to be completely separated from the basement-membrane, and to project into the lumen (Figs. 7, 8 and 9), or, its cells may be seen separating from each other, singly, or in small shreds. In some tubules, finally, the entire epithelium appears broken up, and with the exception of a small number of very faintly colored, or colorless cells, still adhering to the basement-membrane, either in small groups or singly, the whole tubule appears empty.

The cells of the epithelium, however, while undergoing this process of atrophy and disintegration, show as yet no traces of fatty metamorphosis. Most of those, still in contact with the basement-membrane, and, in severe cases, even forming the greater portion in the section, have absorbed carmine, especially their nuclei. But as soon as they are detached from this membrane, their power of absorption diminishes, and they appear but very faintly colored; or even, while the nucleus may still present a feeble carmine tint, the protoplasm of the cell has remained

uncolored. It is not until they separate from each other that their degeneration and disintegration is really perceptible. The destructive process appears to consist in a dissolution or melting down of the hyaline portion of the protoplasm, liberating the granules, which, together with the hyaline substance, finally undergo a fatty metamorphosis (Figs. 11 to 15). At any rate, the granular remains of these cells do, at first, not always present a fatty appearance, though, soon after, the dark contours and the refractive property of the minute granules give sufficient evidence of their fatty nature. Very often, larger or smaller fragments of cells are observed to form a part of these remains, indicating again the grouped arrangement of the granules of the protoplasm, to which I referred in connection with the hepatic cells. In consequence of the breaking down of the protoplasm of the cells, the nuclei are set free, and traveling along with the general mass, they form a part of the resulting infarctions, in which they are almost always observed, either singly, or in clusters. They are then distinguished by being higher colored than the rest of the accumulation.

It is a remarkable fact that, during this process of fatty metamorphosis, taking place in the epithelium of the uriniferous tubules, it is quite rare that larger fat-globules are met with. I have examined a great number of sections for this special object, and have also found larger fat-globules in some of the tubules, especially in those near the capsule; but the number of these instances is so limited that their occurrence may rather be regarded as an exception to the rule. The comparative rarity, or absence, of larger fat-globules may be explained by the constant flow of some urine, even through these obstructed tubules, interfering with their formation. This supposition is corroborated by the streaked, thread-like appearance of the fat as it is observed in the interior of the tubules, particularly directly below the infarctions. Here it appears in long streaks of a yellowish color (Fig. 14), forming quite a contrast to the carmine coloring of the cells. Minute fatty granules, distinguished by their dark contours and high refraction, together with other cellular debris, are observed with these streaks.

In consequence of the degeneration and disintegration of the epithelium, many portions of the tubules are met with entirely denuded of their epithelial lining (*Figs.* 7 and 8, *d*). Although in the convoluted portions this condition is also observed, it is, nevertheless, more frequently found in the smaller tubules; and it is remarkable that not only single tubules are met with stripped in this manner of their epithelium, but generally a whole group or bundle, including descending, ascending, and collecting tubules. The only explanation which I can find for this phenomenon is that these groups represent certain arterial districts. But, even in these empty tubules, epithelial cells, singly or in patches, together with accumulations of granules and nuclei, may frequently be observed. In most instances, perhaps, the empty tubules have preserved their normal caliber, though not unfrequently groups are met with in a collapsed condition, their basement-membrane presenting faint outlines.

Besides the condition of atrophy and degeneration just described, in which the epithelial cells of the uriniferous tubules are found in yellow fever, there is another condition, indicated by a peculiar appearance of a considerable number of cells, and which seems to precede that of atrophy and degeneration. The special description and consideration of this condition, however, I must postpone until I have described the appearance and the nature of the infarctions.

These infarctions, besides differing from each other in composition, are met with in the uriniferous tubules in different conditions. The so-called albuminous cylinders, when examined in an uncolored section, appear under the microscope finely granular, amorphous, faintly glistening, and of a yellowish color. They are, however, studied to a greater advantage in sections stained with carmine, in which, with the exception of the color, they present, especially in transverse sections of the tubules, the same characters. Possessing, as already mentioned, the power of absorbing coloring materials in a very high degree, they appear in such sections very highly colored, and exhibit the carmine tint with a greater brilliancy and intensity than the normal protoplasm of the cells; therefore, when they are met with in their pure condition, that is, unmixed with epithelial fragments and

remains (Fig. 7, *a*), they are easily recognized by their brilliant and even coloring. They generally fill up the whole lumen of the tubule, and mostly terminate in tapering, rounded-off extremities. In most instances, perhaps, they are still surrounded by the epithelium, though not unfrequently they are met with in denuded portions of the tubules, and in direct contact with the basement-membrane. When covered by epithelium, the outlines of the cells may still be recognized, though the whole cylinder appears somewhat darker. Many of these cylinders are found in a broken condition, either simply fractured across, or into a number of greater or smaller fragments of rectangular or polyhedral forms. It is difficult to determine the cause of these fractures, though it may be safely presumed that they occurred by the instrumentality of the knife during the cutting of the sections. In the study of these sections, therefore, the investigator should take this circumstance into account, in order to guard against false conclusions, which he otherwise might draw from his observation. There are, nevertheless, specimens of these broken cylinders here and there met with, of which the fragments appear to have been removed from each other after the occurrence of the fracture, while their angular borders appear slightly rounded, as if washed away by the passage of the urine. Whatever the cause of these fractures may be, they, themselves, at least, give evidence of the brittle nature of these cylinders, which, accordingly, bear resemblance to the so-called "waxy cylinders," frequently met with in interstitial nephritis. A number of these cylinders are observed, which appear distinctly granular in their composition, the very minute granules exhibiting dark contours. Not unfrequently the lower end of the cylinder is in a state of dissolution, when the individual granules may be distinctly seen. And if the very border of the disintegrating extremity is closely examined, some of the granules may almost always be observed exhibiting their fatty nature by their refractive property and dark contours.

Perhaps the greater portion of these cylinders is found to contain epithelial remains, consisting of granules, nuclei, and even entire cells, or their fragments (Fig. 8, *a*). Mostly, their morphological elements of the epithelium are irregularly mixed up into a shapeless mass, but very frequently cylinders are observed

containing, besides the granules, a whole cluster of nuclei, or even entire cells. If these fragmentary remains of the epithelium have, as yet, not undergone the fatty metamorphosis, they appear more intensely colored than the original substance of the cylinder itself, and exhibit very dark contours and a peculiar luster. But not unfrequently instances are met with in which a portion, or the whole, of these epithelial remains have already undergone this metamorphosis, and accordingly appear lighter, or even yellowish, but also with dark contours, especially the granules (Fig. 15, *a*). The degenerated epithelial elements, not enclosed in the cylinder, of course, exhibit distinctly the fatty appearance, as before described. As regards the relative proportion of the albuminous substance of the cylinders with the epithelial remains, it, of course, must differ in every combination of cylinder formed, and be subject to much variation. It may be presumed that the epithelial elements have accumulated in the lumen of the tubule previous to their saturation by the albuminous substance, to which the intense coloring must be attributed. Judging from the tapering form of the extremities of these mixed cylinders, and also from the irregular outlines observed on some of them, they appear to be prone to a gradual liquefaction.

A third kind of infarctions met with in the uriniferous tubules, in yellow fever, are those solely composed of the disintegrated and degenerated epithelial elements. They consist of granular masses of irregular forms, derived from the degenerated cells, and mostly enclosing free nuclei and cells, or their fragments; sometimes, however, clusters of entire nuclei and cells are observed (Fig. 8, *e*). The size or extent of these accumulations is very variable, but it may be stated that, as long as they remain free from being saturated by the albuminous liquid, they never assume the same dimensions as the albuminous cylinders above described, though they are met with in the same localities as the latter. Neither do they appear to become very easily stationary in one particular place of the tubule; on the contrary, being of a softer consistence, and more yielding, and, furthermore, undergoing easily fatty metamorphosis, they are carried along by the pressure of the urine. These epithelial accumulations are frequently observed in a state of fatty degeneration, the whole mass

appearing yellow, or, sometimes, yellowish mixed with brown; in the latter instances the brown color represents hæmoglobin, previously absorbed by the protoplasm of the cells.

Having thus far described the degenerated condition of the epithelium, lining the uriniferous tubules, and the peculiarities of the different kinds of infarctions, formed in the latter during the comparatively brief course of yellow fever, I shall now consider the probable origin and mode of formation of these infarctions, and, moreover, briefly review the existing theories on the subject.

The old theory of the mode of formation o. the so-called albuminous cylinders referred the process to a transudation of the albumen of the blood through the walls and the covering cells of the minute vessels of the glomeruli into the uriniferous tubules, in the interior of which the cylinders were formed by a precipitation of the albumen from the urine This theory is entertained by perhaps the majority of pathologists, though the other, more recent, according to which the cylinders represent a product of secretion from the epithelial cells, or are even the result of a transformation of these cells themselves, is also supported by a number of distinguished authorities. To myself, the old theory hitherto appeared sufficiently plausible to explain the whole phenomenon, though I must confess that an observation which I made during these studies on a considerable number of epithelial cells, to be described hereafter, has induced me to view the more recent theory in a different light. Let us, therefore, examine both sides of the question.

As the old theory is sufficiently understood to pass without further explanation, I shall, in support of it, only cite the views of *Runeberg*,* one of the more recent investigators into the pathogenetic condition of albuminuria. They are as follows: "The transudation of serum albumen always takes place in the glomeruli. It is conditioned by an increased permeability of the walls of the looped vessels of the glomeruli and of the epithelium covering them. In consequence, the particles of albumen suspended in the serum of the blood, which under normal conditions

* *Virchow u. Hirsch*, Jahresbericht etc., für das Jahr 1878, Vol. 1, p. 219.

are unable to pass through the membranes of the glomeruli, may now in part be filtered with the remaining constituents of the urine. This increase of permeability is, in otherwise healthy kidneys, already caused by a considerable diminution of the difference between the pressure of the blood inside the glomeruli and the counter pressure existing in the uriniferous tubules. The accidental or transitory albuminuria is, therefore, conditioned by a considerable augmentation of the presence of the blood in the glomeruli, or by a diminution of the pressure in the tubules, or by both of these circumstances. In the permanent albuminuria, however, increased permeability of the filtering membrane is conditioned by an inflammatory or degenerative process affecting the vessels of the glomeruli; but, even here, the permeability is perceptibly influenced by the relative amount of pressure, and, in the same direction, also the amount of albumen in the urine, as explained before. A part of the albuminous substances, as the egg albumen and the hæmoglobin, are in a higher degree filterable than the serum albumen. As soon, therefore, as these substances are, in any way, mixed with the serum of the blood, they at once, even under normal conditions of the pressure of the blood, filter into the urine like the soluble salts."

The more recent theory, according to which the cylinders represent a product of secretion from the epithelial cells of the uriniferous tubules, or result from a transformation of these cells themselves, has been advocated by *Oedmansson*, *Axel Key*, *Oertel*, *Rovida*, *Senator*, *Heynsius*, *Bayer*, *Birch-Hirschfeld*, *Aufrecht*, and probably by a number of other pathologists. I shall cite the views of some of these authors. Thus, *Rovida** who subjected the urinary cylinders to an extensive chemical examination distinguishes three particular kinds, the *colorless*, the *yellow*, and the *epithelial*. As regards the chemical nature of the colorless, and the yellow or waxy cylinders, he says, that they do not represent albumin, or an albuminate, nor one of the known bodies derived from albumen, although they chemically resemble the latter substances.

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* l. c.—für das Jahr 1872, Vol. I p. 206.

He states a case of diffused nephritis without contraction or amyloid degeneration of the kidney, in which, beside colorless and yellow cylinders, numerous yellowish minute scales, exhibiting a similar luster as the latter, had been observed in the urine during the life of the patient. The same elements were met with in the fresh kidney, when microscopically examined after death. After the organ had been hardened in Mueller's fluid and in alcohol, the epithelium of the convoluted tubules appeared turbid and granular, so that the nuclei could scarcely be distinguished; the lumen was filled up, partly with homogeneous, partly with slightly granular globules of the same color and refractive as the yellow cylinders. In many uriniferous tubules, spherical drops of yellow color were observed, especially in transverse sections, to project from the epithelium; they were also found, here and there, in the lumen, partially collected into irregular polyhedral figures. In other places they formed an almost spherical contour, blending toward the center with a firmer, more compact mass, which, filling up more or less perfectly the lumen of the uriniferous tubule, represented a yellow urinary cylinder. From this observation, Rovida concludes, that the yellow cylinders, also, are products of secretion from the epithelium of the uriniferous tubules, the same as had been previously shown by Oedmansson, Key, and Oertel in connection with the colorless cylinders. But, finding in the same kidney, in some places, especially in the descending and ascending tubules and in the loop of Henle, the epithelium yellowish and more refracting, he agrees with Key, in admitting that the cylinders may also be formed by a fusion of transformed cells.

Senator,* who also made numerous investigations upon the albuminous bodies in the urine, regards albuminuria as depending upon an abnormal circulation. The increase of tension which the vessels of the glomeruli experience during a general venous congestion, he thinks, is inferior in degree to that of all other capillaries, while at the same time the secretion is diminished by an accumulation of the secreted matters in the uriniferous tubules. In addition, a diminution of the arterial pressure,

* l. c.—für das Jahr 1874, Vol. I, p. 342.

as usually observed during venous congestion, occurs. Therefore, the albumen cannot be regarded as a product of filtration from the glomeruli, but is probably derived from the interstitial vessels bearing high pressure. In pure cases of amyloid degeneration, the urine voided from the Malpighian canals must be regarded as a mixture of a serous, non-inflammatory transudation, pressed through the glomeruli. The changes, occuring in the different forms of diffused, interstitial and parenchymatous nephritis in the urine, are depending upon the effects of the changed afflux and reflux of the blood in the vessels of the glomeruli, and in the interstitial vessels, and from those caused by the accumulation of secreted matters in the uriniferous tubules. The albuminous cylinders Senator regards as a product of a disturbance of nutrition of the epithelium

Heynsius,* who closely investigated the same subject, agrees with Senator in the following points : namely, that the albuminous bodies met in the urine need not resemble those of the plasma of the blood in all points ; that the epithelium of the kidney undoubtedly possesses some influence over the secretion in general, and over that of the albumen in particular ; and that the cylinders are not formed by transudation from the plasma of the blood, but are rather derived from the protoplasm of the epithelium.

The cause of albuminuria, he thinks, may be found not only in an increased venous pressure, but also in a diseased condition of the epithelium of the uriniferous tubules, in consequence of which the quantity of albumen, transuding through the vessels in the normal condition, is not consumed for the nutrition of the epithelium. The destruction of the latter, however, causes a diminution of the acid reaction, followed by an increase in the quantity of albumen.

Birch-Hirschfeld † adopts the view of Key, according to which the hyaline cylinders are probably formed by a secretion of the epithelium, while the granular cylinders are formed by a fusion of the degenerated epithelial cells.

Aufrecht ‡ found that in the rabbit, after ligation of the ureter on one side, a granular turbidity of the epithelial cells in the

* l. c. p. 213.
† *Birch-Hirschfeld.*—" Lehrbuch der Pathologischen Anatomy," 1877, p. 1038.
‡ *Virchow u. Hirsch*, Jahresbericht, etc., f. d. Jahr 1878, Vol. I, p. 222.

cortical substance of the kidney of the same side, associated with the formation of cylinders takes place, followed—about six days after the ligation—by a proliferation of cells in the interstices of the uriniferous tubules. He agrees with Oedmansson, Axel Key, Senator, and others, that the cylinders are formed by the irritated epithelial cells, and represent a secretion, which, in several instances, he has seen projecting from the cells.

Having thus briefly reviewed the leading theories on the formation of the albuminous cylinders, and, moreover, cited the particular views of some of the investigators, I shall now proceed to state my own observations on the subject. In the preceding description of the condition of the epithelium of the uriniferous tubules, the degree of degeneration in which the cells were found, was, as will be remembered, determined by the capacity of absorption which they showed for coloring matters. In accordance with this test, those least, or not at all, degenerated, exhibited a perfect staining, while others were more imperfectly colored, or had remained entirely colorless. These cells, moreover, without reference to the quantity of carmine absorbed, did not present any lustrous or glistening appearance, nor that intense color exhibited by the urinary infarctions. There are, however, a considerable number of others, as yet not mentioned, met with in all sections of yellow fever kidneys, which do present *the same intense color and glistening aspect as the infarctions.* They are particularly well exhibited in transverse sections of the uriniferous tubules in which the epithelium appears in the form of a ring, though they are also distinguished in others, or even in the entire tubule through the basement-membrane. In many instances, only a certain number of the cells, forming the ring, present this peculiar appearance (Fig. 9), though in others, all the cells of the epithelial ring appear affected (Fig. 10).

These deeply colored and glistening cells are not confined to any particular locality, but are met with in all portions of the tubules. Neither are they confined to particular cases, for I observed them in all the sections I examined, and without reference to the greater or lesser extent of the destructive changes in the parenchyma of the kidney. They were rather more frequently observed in the milder cases, in which the process of

degeneration was of a limited extent. In such cases, I also observed this characteristic appearance on a number of cells, lining some of the collecting tubules, and which showed no signs of atrophy or degeneration besides (Fig. 10, *a*), but had preserved their normal size and form. In some of these sections, no cylinders of notable size were found; those met with were contained in the smaller tubules and very short. In these instances, however, a number of transverse sections of the smaller tubules were also observed, in which not only the epithelial ring exhibited the deeply stained and glistening appearance, but in which the lumen was moreover filled with a cylinder (Fig. 10 *b*), presenting the appearance of being blended with the ring, such as was observed by Rovida in the uncolored specimen.

It will be obvious that these observations strongly corroborate the more recent theory, according to which the albuminous cylinders are a product of secretion from the epithelial cells of the uriniferous tubules, or may even be formed by a fusion of the degenerated cells themselves. Some additional remarks, however, will be required to render the probable correctness of this theory more comprehensible. It has already been mentioned that in many transverse sections of the albuminoid cylinders, unmixed with epithelial remains, the epithelium is found perfectly intact, and, though decreased in its normal thickness, nevertheless appears evenly colored, showing the absence of fatty metamorphosis. This fact has been advanced by *Weissgerber* and *Perls*,* for the purpose of showing the fallacy of the theory in question, but loses its significance if explained in another way. These investigators probably supposed that if the cylinders were a product of secretion from these cells, the latter should still contain a portion of this product, and accordingly present the same yellowish and glistening aspect as the cylinders. This condition of things, it is true, may be conjectured, and I presume does, in some instances, exist, and may sometimes also be observed, though its actual observation is by no means essential; for, having observed the deep color and glistening appearance on the cells of collecting tubules—in some instances on the entire epithelial ring—which had preserved their normal turgescent form, I am

* l c.—fuer das. 1876.—Vol. 1, p. 263.

inclined to regard this abnormal secretion as the initial stage of the degenerative process, followed, directly after the discharge of the secreted product, by the atrophy of the cells, before mentioned. It is, therefore, not essential that the cells surrounding a cylinder, representing the discharged product of their secretion, should in all cases still present the optical characters of this product; on the contrary, after the complete discharge of the secretion, they may not only resume their former appearance, but at the same time appear atrophied by the loss of material. But even if this supposition were wrong, there remain other probabilities of the cylinders being in truth a product of secretion; for it is not essential that this product should have come from those particular cells by which it is surrounded. On the contrary, it is more likely that it has been secreted from cells situated higher up, and, being at the time of secretion in a semi-fluid condition, has descended until arrested by the ensuing coagulation at another part of the tubule, in which the epithelial cells have not been similarly affected.

In some instances, as has been mentioned, the epithelium, generally surrounding the cylinder or infarction, has entirely disappeared, the latter being in direct contact with the basement-membrane. In these cases it may be presumed that these infarctions, consisting of epithelial remains saturated with the albuminoid matter, were probably formed in the place where they are found, while purely albuminoid cylinders are derived from cells situated higher up in the tubules.

It has already been noted that, in some instances, the minute vessels of the glomeruli were found filled with blood-corpuscles, showing that the congestion had extended throughout the whole capillary network of the interlobular vessels; generally, however, the vessels of the glomeruli were empty, and appeared normally colored; in a few instances they even appeared contracted, and the glomerulus diminished in size. In examining a considerable number of sections for the special purpose of discovering the peculiar condition of the epithelial cells above described, also on the layer of cells covering the vessels of the glomeruli, I only succeeded in observing in some parts of a few glomeruli the deep coloring and glistening appearance; besides this, I also met with

the segments of a few capsules, upon the inner surface of which an exudate, moderately colored by the carmine, could be detected. Another observation, however, quite as interesting, consisted in the presence of fat-globules, such as might be derived from a fatty infiltration, in a number of the cells of the covering epithelial layer of many glomeruli. These observations show that these cells also are prone to be affected in the same manner as those lining the uriniferous tubules.

As in the liver and stomach, so in the kidney, extravasations of hæmoglobin take place from the capillary vessels, to be absorbed by the epithelial cells of the uriniferous tubules. Almost in every section of yellow fever kidney, some traces of free hæmoglobin, recognized in carmine preparations by their peculiar brown color before mentioned, may be observed in any portions of the tubules. Sometimes the extravasation is observed in a considerable number of neighboring tubules. The pigmentation, however, is not confined to the formless hæmoglobin, for hæmatoidin in granular or crystaline form is also met with. Hæmatoidin crystals, especially, are frequently seen upon the inner surface of the epithelium, generally collected in small groups or masses of very minute crystals, though in one particular case I also observed numerous granules of hæmatoidin in the interior of a number of empty uriniferous tubules. The brown color which the epithelial cells assume by the absorption of the hæmoglobin, of course, differs in intensity in different localities, according to the quantity absorbed. These extravasations are not limited to kidneys extensively degenerated, but are equally observed in cases presenting only slight traces of the degenerative process.

As far as my experience extends, there is no product of inflammation found in the yellow fever kidney. Although I had, in every section examined, my attention directed to this point, I failed to discover any trace of such a product, either in the vicinity of the connective tissue capsule, or in the interstitial tissue. Therefore the destructive changes occurring during the course of yellow fever, in the parenchyma of the kidney, are the result of hyperæmia.

In conclusion, I may remark that no traces of bacteria, or other minute organisms, could be discovered in this organ. If such

organisms were really present in the kidney, as has been erroneously stated, we should most probably find them in the minute blood vessels, or in the interior of the uriniferous tubules. But not a single specimen, or colony, have I met with in these localities in the very numerous sections which I have examined. And if ever these organisms are met with in these places, a close investigation will certainly show that they were developed along with the decomposition of the body, or of the kidney itself, after its removal from the former. In one exceptional case only, I observed upon a section, mounted in Canada balsam, one or two granular patches, representing colonies of minute micrococci. A change of the focus, however, showed that they were not contained in the preparation, but were simply resting upon its surface, where they had been developed after the section had been cut, an accident which probably occurred in the staining fluid, or while the sections were kept in a mixture of alcohol and water, previous to the process of mounting.

THE SUPRA-RENAL BODIES.

These organs, of which the true function is, as yet, not known, are in fatal cases of yellow fever almost invariably found to have undergone certain pathological changes. To render a description of these changes more perspicuous, we may, as before in some other instances, briefly review their microscopical anatomy.

As in the kidney, so in the supra-renal bodies, a "cortical" and a medullary substance have been recognized—though here no secretory ducts exist, but both substances consist of minute blood vessels and cells, supported by a fine reticulated network of connective tissue. This network originates by certain septa, or processes, arising from the inner surface of the general capsule of the organ, whence it extends throughout the parenchyma, to be finally connected with the adventitia of the veins, which leave the organ through its hilus. The blood-vessels of the organ are very numerous, and represent branches of the aorta, and of the phrenic, cœliac, and renal arteries, which, after penetrating the capsule, subdivide into numerous minute branches, terminating in the capillaries of the cortical substance. Three distinct layers of cells are distinguished in this substance. The middle one of

these layers truly represents the bulk of the cortical substance, while the outer and inner ones only appear as narrow borders. The inner layer blends with the adjoining medullary substance. The cells, which are polygonal or round in form, occupy the space between the septa in the form of larger or smaller groups or columns. In the outer and inner layer, these groups, in accordance with the smaller and rounder meshes of the reticulum, are small and of a roundish form, while in the middle layer, in which the meshes are larger and much longer, the groups of cells assume the forms of columns. The medullary substance consists of a reticulum of very delicate connective tissue, with small meshes, filled up by small groups of polygonal or stellated cells, containing large nuclei. The capillaries, differing in their caliber in the different localities of the parenchyma, generally follow the septa and columns of the reticulated connective tissue, and, accordingly, the form and size of their meshes correspond with those of the meshes of the reticulum. Their caliber is of a medium size in the cortical substance, but in reaching the medullary substance, in which they represent a network with small meshes, they considerably enlarge in diameter, and many of them even present dilatations. In the latter network, the venous radicles take their origin. The nerves in the supra-renal bodies are very numerous; they are derived from the semi-lunar ganglion, the renal plexus, and the phrenic and pneumogastric nerves, and, after having entered the organ, are chiefly distributed to the medullary substance, forming plexuses in connection with which ganglion-cells have also been observed. The pathological changes observed in the supra-renal bodies resemble those taking place in other organs already described, consisting in the infiltration of fat and hæmoglobin, derived from the blood, and preceded by hyperæmia of the organ. In most cases, therefore, the examination of thin microscopical sections shows the capillaries filled with blood-corpuscles, especially those larger ones extending through the medullary substance, though in a number of cases I also observed the others, particularly those of the outer layer of the cortical substance, congested. The fat-globules, resulting from the fatty infiltration, are quite large, and are found in the cells of both substances, though perhaps to a greater extent in the cortical.

The infiltration or extravasation of hæmoglobin absorbed by the cells is greater and more general here than has been observed in any other organ. Almost in every case examined, it involved the whole medullary substance, from which it extended into the inner and middle layer, sometimes even into portions of the outer layer of the cortical substance. The degree of this pigmental infiltration is sufficiently great to be always distinguished by its brown color in sections of fresh specimens; in some cases, even, it appears dark brown. In sections, stained with carmine, the infiltrated cells exhibit the characteristic brown color of the extravasated hæmoglobin, already referred to. Besides the fatty and pigmental infiltration met with in every specimen examined, I moreover observed, in some cases, that a process of atrophy of the parenchymatous cells, particularly those of the medullary substance, had also been going on. In some cases, even, the atrophy was associated with softening of this substance, which presented a dark brown color; the softening process had given rise to a cavity in the organ. The atrophy appeared to be chiefly confined to the protoplasm of the cells, the nuclei remaining unaffected.

For the sake of comparison, I prepared a number of sections of supra-renal bodies taken from several cases representing other diseases than yellow fever, such as of the heart, liver, kidneys, and lungs. In these sections, a trace of pigmental infiltration was detected, but too insignificant to be in any way compared with that observed in yellow fever, as it was entirely limited to a very narrow yellowish brown stripe, representing the inner border of the cortical substance.

Although a number of pathological conditions and structural changes, such as hypertrophy, atrophy, fatty and amyloid degeneration, suppurative inflammation, carcinoma, tubercle, cysts, and even extensive hæmorrhages in the interior of the organ, have been observed to occur in the supra-renal bodies, I have thus far seen no record of an infiltration of hæmoglobin into the parenchyma in such a marked degree as I have observed to take place in yellow fever,—a phenomenon to which some special signification regarding the normal function of these organs might be attached, if it was not simultaneously observed in the liver, stomach, and kidney. For this reason, it must be regarded, as

in the other cases, depending upon the hyperæmic condition of the vessels, retarding the circulation of the blood through the latter. The fatty infiltration, also, is evidently due to the same general causes, from which it depends in the other organs already mentioned.

THE CEREBRO-SPINAL AXIS.

The Pia Mater.—In connection with the macroscopical examination of the organs after death, I stated that this membrane, as far as it extends over the brain, was almost invariably found in a state of hyperæmia, and that, in many cases, not only the veins, but also the arteries were found filled with blood. The microscopical examination reveals the same condition in the minute vessels, the arterioles, venules and capillaries. In examining, therefore, a small piece of pia mater, carefully removed from the cortex cerebri, these vessels, with only a few exceptions, are, in most instances, found more or less filled with blood corpuscles; in some of them, even, the corpuscles are crowded to such an extent as to have lost their original form by the mutual pressure which they had exerted upon each other. In removing the pia mater, the minute vessels entering the substance of the brain are, of course, torn, causing the blood corpuscles which they contain to escape. The stumps of these vessels, appearing like villi, and attached to the inner surface of the membrane, are usually found empty. Notwithstanding the intense hyperæmia which appears to have existed during life in many portions of the pia mater of the brain, I have, with one single exception, failed to detect any exudation cells in the vicinity of the vessels, or any increase in the connective tissue cells of the membrane, which might have indicated the pre-existence of inflammation,—a fact, which clearly shows that the cerebral phenomena observed at the bedside, are the results of a simple though severe hyperæmia. In the one exceptional case, the connective tissue cells had just commenced to undergo a division, resulting in a small group of three or four cells, or only nuclei, in the place of the old ones (Fig. 17). In some cases, I have observed that the walls of a number of arterioles, especially of those which are empty, or containing but few blood corpuscles, presented a corrugated or wrinkled appearance. As the wrinkles were confined to the

adventitia, they appear to have been caused by a contraction of the delicate muscular fibers, encircling these small vessels. If this be the true cause, the contraction must have occurred before death, or during the agony of death itself. But there is another pathological condition, which, in fully one half of the cases examined I observed to have taken place in these minute vessels, both arterioles and venules, and which consisted in a fatty degeneration of their nuclei, especially of those belonging to the adventitia. In most of these instances, the nuclei have disappeared, leaving a group of smaller or larger fat globules in their places. In other instances, an increase in the mere trace of protoplasm, found in connection with the nucleus in its normal condition had taken place, causing a thickening of the wall of the minute vessel, and giving rise to a capillary aneurism, or, by its proneness to degeneration, even to a final rupture followed by hæmorrhage. The small hæmorrhagic effusions, observed in some of these cases, may have been owing to this cause.

The arachnoid membrane, as before stated, is very frequently found not only opaque, but also thickened. This condition is caused by an exudation of a finely granular matter into the subarachnoid space, filling up, at the same time, the meshes of the connective tissue of the pia mater. The granules of which this substance is composed, are quite distinct, but pale, and measure about $\frac{1}{1200}$ mm. in diameter. In the pia mater of some cases, and mostly in the close vicinity of a vessel, or associated with a minute hæmorrhagic effusion, smaller or larger brownish looking granular masses of irregular form, are here and there observed. The granules of these masses are identical with those of the exudate before mentioned, though they appear more distinct, which is probably owing to the presence of free hæmoglobin, imparting the color to the mass. A number of similar, but colorless granular accumulations are moreover observed in the spaces between the vessels. It is quite probable that these accumulations represent minute portions of granular substance from the upper stratum of the cortex cerebri.

The hyperæmia of the pia mater is not confined to those portions of the membrane covering the cerebrum and the cerebellum, but, moreover, extends over the pons varolii and medulla oblon-

gata, frequently even as far as the cervical enlargement of the spinal marrow. In many cases, the congestion of the vessels of the pons and medulla is greater than that of the central vessels.

While in the cervical and dorsal regions, the pia mater of the spinal marrow is generally found free from congestion, its vessels are almost always found filled with blood corpuscles in the lumbar region. This fact can be sufficiently demonstrated in thin sections of spinal marrow from this region, in which the minute vessels of the membrane, with those that enter the spinal marrow, are observed filled with blood corpuscles.

The Substance of the Brain.—As it may well be asserted, that in yellow fever the safety of the patient almost entirely depends during the febrile stage, and after, upon the particular condition of the nervous system, especially the brain, an exact knowledge of the pathological changes taking place in this organ, are most important. And, judging from the traces of intense hyperæmia, met with in almost all fatal cases in the pia mater, as above described, we may well expect to find a similar condition in the substance of the brain. The pathological condition of this organ may be studied to the greatest advantage in large thin sections, passing through the whole extent of its different parts. The examination of a very great number of such sections revealed to me that, in almost every case examined, the hyperæmia extended from the pia mater *throughout* the substance of every portion of the brain. Not only the arterioles and venules were found filled with blood corpuscles, but also the capillaries. In most instances, the blood corpuscles are crowded in the arterioles and venules, and to such a degree as to have lost their normal form by their mutual pressure. In the pons varolii and medulla oblongata particularly, the vessels are invariably found filled with blood corpuscles, inducing me to regard these parts as special seats of the congestion. In some cases, I have even found opacity of the pia mater covering these localities. In those cases in which there was fatty degeneration of the arterioles and venules of the pia mater, this process is observed to have extended to the same minute vessels of the brain substance. In some cases, even, I observed traces of commencing degeneration in a considerable number of ganglion cells, especially on those of

the cortex cerebri, but also in the medulla oblongata. While in a normal ganglion-cell, namely, the double contour of the nucleus, and the outlines of its granules and those of the protoplasm of the body, generally seem distinct, they here appeared indistinct, and the whole ganglion cell presented a fatty luster. This condition is best observed in uncolored sections, examined in water or glycerine. In one case, I observed that though the outlines of these anatomical constituents of the ganglionic bodies of the cortex cerebri had been well preserved, their protoplasm had undergone atrophy, reducing their size. Notwithstanding the occurrence of extravasations of hæmoglobin in every other organ examined, the pia mater not excepted, as I have shown before, the substance of the brain appears to be remarkably free from this pigmentary infiltration; neither were in all the cases examined microscopically—about a dozen—capillary hæmorrhages met with.

As regards the *spinal marrow*, there are, aside from the congestion of the vessels of the pia mater above mentioned, no pathological changes observed in the nervous elements.

THE GANGLIA OF THE SYMPATHETIC NERVOUS SYSTEM.

The microscopical examinations which I made on these ganglia, embraced a very considerable number of sections, made of the *first thoracic*—G. stellatum—and the *semi-lunar* ganglia of six cases. In the majority of these cases, the minute blood vessels of these ganglia were found filled with blood corpuscles. In two cases, the ganglionic bodies of the first thoracic, as well as of the semi-lunar ganglion, had most obviously undergone degeneration. In the greater part of these ganglion cells, the nuclei had entirely disappeared (Fig. 16), leaving no other trace but their nucleoli, which appeared very distinct; in the rest, *very faint* outlines of the nuclei could be still observed. The bodies of all these ganglion cells presented an indistinct appearance, and were characterized by a peculiar fatty luster, even observed on specimens mounted in Canada balsam. As there were no fat globules observed in the places of the nuclei, it is difficult to account for their disappearance, unless it was caused by a process of atrophy, such as was observed to occur on the epithelial cells of the

uriniferous tubules. In a third case, I observed an abnormal accumulation of pigment in a considerable number of ganglion cells of the semi-lunar ganglion. In the three remaining cases, nothing specially abnormal could be detected on the ganglion cells.*

The preceding description of the pathological changes taking place in various organs and tissues in the course of yellow fever, is based upon very numerous and careful examinations, made during former epidemics, but particularly upon the abundant material which I collected during the epidemic of 1878. In the pursuit of these studies, portions of the organs were examined in their fresh condition directly after the autopsy, while the rest were put into a simple solution of bi-chromate of potassa, or into Mueller's fluid. A few days later, after the tissue had been slightly hardened, the examinations were repeated upon thin sections made by the free hand; but after they had attained the proper consistency, larger and perfect sections were made by the aid of the microtome. These, finally, were carefully prepared, stained, and mounted in Canada balsam or glycerin, in order to serve for the more thorough final studies.

The amount of material which I have in this manner examined and studied is very great; it embraces the various organs of twenty-three cases out of the thirty autopsies which I made during the epidemic of 1878, and those of an additional most interesting case in 1879. I have made more than two thousand thin sections, ranging from the larger ones, passing throughout an entire hemisphere of the cerebrum to the smaller of the sympathetic ganglia, or the mucous membrane of the stomach. The

* In the "Report of the Havanna Yellow Fever Commission of the National Board of Health," it is stated that in the semi-lunar ganglion "connective tissue of new formation is met with to a greater extent than in the tissues heretofore described, but the nervous elements present no evidence of degeneration further than the cloudy swelling already described in other organs; while of the other portions of the nervous system which have not been examined microscopically, it may be said, that they present nothing abnormal to the naked eye."

The discrepancy existing between these statements and my own observations, I can only explain by presuming that the pathological expert of the commission took the very numerous nuclei, belonging to the capsules, and to the intricate extensive plexuses of sympathetic nervous fibrillæ connecting the ganglionic bodies, or to the bundles of sympathetic nerve fibers arising from them, for newly formed elements. As regards the report of the condition of the other portions of the nervous system, I could only infer that the type of yellow fever at Havanna must differ from that observed at New Orleans.

sections of the brain are especially numerous, comprising all parts of the organ, and representing a considerable number of cases. About one thousand of these sections, taken from different organs, I have mounted in Canada balsam or glycerin, a large portion of them being in the possession of medical friends in New York, Philadelphia and Chicago, while the rest remained in New Orleans.

A word concerning the mounting and examination of these or similar specimens may be advisable here, as their successful study much depends upon the medium in which they are examined. Thus, though the mounting in Canada balsam is the most substantial and beautiful for colored sections of tissue, there are nevertheless certain disadvantages connected with this medium, and depending upon its high degree of refractibility. This is the case with tissues that have suffered fatty infiltration or degeneration, in which the fat globules, by the too great amount of light passing through them, are rendered quite indistinct, and difficult of recognition. For this reason, it is better to examine and mount such specimens in a less refractive medium, such as glycerin. In examining stained tissues, mounted in balsam, they should not be too brilliantly illuminated, as too much light will render indistinct the image of structure, though it shows well the image of color. It is more advantageous, therefore, to use the plane mirror and a small diaphragmatic opening for the sections mounted in balsam, while the glycerin sections may be examined with the concave mirror. I need hardly mention that examinations of this kind should only be made with the very best first-class objectives, as an inferior objective does not show the details in their true light.

GENERAL PATHOLOGY.

We have now studied the clinical phenomena of yellow fever, together with the pathological changes taking place in various tissues and organs during the course of the disease, and revealed by a post mortem macroscopical and microscopical examination; a comparison of these two sets of phenomena with each other, for the purpose of determining, as far as possible, the relationship necessarily existing between them must, therefore, be the next object in view. Formerly, when diseases were classified by certain groups of clinical phenomena, or symptoms, which they presented, it was chiefly these symptoms to which the physician directed his attention, and by which he was guided in his treatment, consisting for the most part of remedies to which, in the cure of each particular disease, a specific action was attributed. With the rapid development of pathological science, however, the custom of treating disease in this empirical way was gradually abandoned for more rational methods, based upon a thorough knowledge of the intrinsic nature of the disease, obtained from the nature of the pathological changes observed after death in the tissues and organs. But even a knowledge of these changes, wrought upon the internal organs by the morbid process of one or the other disease, is insufficient to safely guide the physician in his efforts to obtain a cure, unless he is able to tell from the symptoms, presented by the particular condition of his patient, the exact and simultaneous condition of these organs; in other words, to form an accurate scientific diagnosis, the highest accomplishment of the practicing physician. In a considerable number of diseases, especially those of the heart and respiratory organs, medical science has reached this aim, and I am confident that, to a considerable extent, the same may also be accomplished in yellow fever.

In yellow fever, as in other acute infectious diseases, the most prominent phenomenon observed is that of fever; I shall, therefore, introduce my remarks on the general pathology of this

disease with a brief consideration of the observed facts, relating to the *febrile process in general.*

Various theories on the phenomenon of fever have been advanced by medical men at all periods of medical history. The older theories were all based upon the principles of "humoral pathology," according to which not only fevers, but all other diseases depended upon a contamination of the blood, caused by the reception of noxious substances from without, or, in consequence of certain changes going on within the body, the febrile process being an effort of nature to expel the noxious matter. It was *Hoffmann*,* who first directed the attention from the fluids to the solid tissues, as the seat of the disease. He sought the source of fever in the nervous system, believing that it was originally depending upon a spasm of the capillaries, and considering the heat of the skin and the arterial excitement which follow as the mere reaction of the system, necessary to overcome this spasm. A very similar theory was entertained and promulgated by *Cullen*, and, also, in a more or less modified form, by some other authors. Another theory of fever was, in the beginning of this century, put forth by *Clutterbuck*,† who regarded all forms as of local origin, and depending upon local inflammation. The so-called idiopathic fevers, therefore, he regarded as inflammation of the brain, designating them "encephalitis." *Broussais*, in announcing his doctrine of fever, agreed with Clutterbuck in denying the existence of essential fevers, but differed from him in ascribing all those forms, previously denominated idiopathic, to inflammation of the mucous membrane of the stomach, or that conjointly of the stomach and bowels; in other words, being *gastritis* or *gastro-enteritis.* The impression which Broussais's theory had made, gradually faded, and there has been no doctrine of fever since which had a general prevalence, though the above theories of fever have, with various modifications, extended into our time. Thus, the neuro-pathological theory of Hoffmann and Cullen was, in a modified form, subsequently more developed by *Virchow*,‡ who regarded the phenomena of the febrile process,

* *G. B. Wood*, "Practice of Medicine," fourth edition, Vol. I, p. 101.

† L. c., page 103.

‡ *R. Virchow.*- Handbuch der Pathologie u. Therapie, 1854, Vol. I, p. 33.

especially the elevation of temperature, as depending upon a depression (Nachlass) of certain parts of the nervous system, which he supposed to act as moderators of the production of heat. In still more recent times, however, the old theories based upon humoral pathology, appear to recover their lost grounds.

Although the most prominent symptom of fever, the abnormally increased heat of the body, has always been attributed to an increased waste of matter derived from the tissues, the discovery of a correspondingly increased formation of urea, found in the urine during the febrile process, and verifying this supposition, belongs to more recent times. The precise nature of the febrile process itself, and the true cause of the increase of bodily temperature, however, remained still unknown, and gave rise to very numerous and laborious investigations, made by a considerable number of investigators, such as *Jochmann*, *Traube*, *Moos*, *Redenbacher*, *Uhle*, *Ringer*, *Brattler*, *Wingl*, *Wachsmuth*, *Warnecke*, *Huppert*, *Tschsschichim*, *Breuer*, *Chroback*, *Leyden*, *Ranke*, *Senator*, *Naunyn*, *Unruh*, and others.* A most able treatise, covering the whole subject, and embracing his own labors as well as those of others, was written by *Senator*,† who, for his extended contributions to the knowledge of the febrile process, as far as it goes, may be regarded as a prominent authority. And as some of his special views seem to have been corroborated by still more recent observations, I shall not hesitate to extract from his treatise in the following discussion.

In the above mentioned investigations, the attention was particularly directed to the existing proportion between the production and discharge of heat, carbonic acid and water; and the most prominent facts thus far elicited were: an increased formation of urea in the urine, and an augmentation in the discharge of carbonic acid, water and heat.

The increased formation of urea is not depending upon a greater activity of the normal exchanges of matter in general, but rather upon a greater waste of albumen. The quantity of urea excreted during the whole fever amounts in the average to

* *Virchow u. Hirsch*, Jahresberichte, etc., für die Jahre 1866–1872. Section: Allgemeine Pathologie.

† *Senator.*—"Untersuchungen ueber den Fieberhaften Process, und seine Behandlung." Berlin, 1873.

more than twice the quantity excreted during the absence of fever, but otherwise under the same conditions; that is, when the body is kept on fever diet. The average quantity of urea excreted on such diet, and taken by Senator as a basis, was 18 grms. in twenty-four hours.

The increase in the quantity of urea secreted begins, as was first observed by Ringer, Traube, Joachmann, Uhle and Redenbacher, before an elevation of the bodily temperature is noticed. Senator, who corroborated this fact by his experiments on dogs, in which, contrary to man, the activity of the urinary function increases during the febrile process, enlarges upon this phenomenon as follows: "Whilst, namely, with the dog the quantity of urea discharged with the urine in about twenty-four hours may be looked upon as equal to that *formed* in the same time, such a presumption is not accepted as regards most febrile diseases in man. In the dog, at least in artificially produced pyæmia, the discharge of urea is favored by the augmentation of the water of the urine; and a loss of nitrogen by some other way than through the urine, as, for example, through the fæces, did not take place during the time of observation. With man it is different. Here, the amount of urine is usually diminished, and with this the chief source for the abstraction of nitrogen is limited. In consequence, the removal of the latter does not keep equal pace with the extensive disintegration of albumen; urea—or, as we may for the present suppose, bodies formed preliminary to urea—accumulate in the body, to be afterwards eliminated at a shorter or longer time after the defervescence of temperature, as the post-febrile augmentation of the discharge of the urea so frequently shows. Besides this, the last residue of oxydized nitrogen is certainly as yet not removed with the latter, but even in the succeeding days the origin of a portion of the discharged urea may still be referred to the time of fever. Moreover, the post-febrile augmentation of urea does not always show itself very conspicuously, as, quite frequently, the body rids itself of its surplus only very gradually, and an imperceptible transition from the febrile to the normal excretion of urea takes place, so that it is difficult to determine how far this is still depending upon the influence of the fever." He further remarks that in different

febrile diseases, much nitrogenous material, in various other forms than the ordinary constituents of urine, leaves the body, or, at least, is abstracted from the exchanges of matter, not only with the stools, but with the expectoration, or in the form of albumen in the urine, as it frequently occurs with high temperatures. These losses, which affect the organism only during the fever, but not when in a state of inanition, also bear in favor of a febrile augmentation of the exchange of albumen ; for, if these quantities of nitrogen were not abstracted from the exchange of matter, the organism would discharge still more urea during the fever. According to *Hoppe*, the quantity of ammonia in the urine, also, is considerably augmented in febrile diseases forming an expenditure of nitrogen not taken as yet into account in determining the quantity of urea. If, therefore, in the fever of the dog, the augmentation of the excretion of urea may be regarded as in just proportion to that of the disintegration of albumen, this is not applicable in the same degree to man. On the contrary, the disintegration of albumen during the fever of man is augmented in a greater measure, as can be calculated from the increase of the urea, and must, therefore, amount to more than double the exchange taking place under the same conditions without fever.

The conditions for the discharge of carbonic acid are, according to Senator, during the hot stage of the fever better than normal; under the most favorable circumstances, the discharge during the day time is augmented from thirty to forty per cent., while during the night, it is probably, as in the normal condition, generally less. The formation of carbonic acid during fever, therefore, can, in the most favorable case, only augment to below thirty to forty per cent.

From the above facts, Senator concludes that in the fever of man no uniform augmentation of the whole exchange of matter, viz., the albumen and fat, takes place. As regards the disintegration of the constituents of the body during the febrile process, however, there are other facts known, which not only confirm it, but moreover indicate, which particular tissues are affected by the augmented disintegration. Above all, it is the exact investigations of *Salkowski* upon the excretion of the alkaline salts, which have shown that the quantity of potassa excreted by a

healthy individual on fever diet, is from three to four, or even seven, times augmented during the febrile process, while a similar augmentation of soda does not take place. The latter, on the contrary, appears to be excreted in a smaller quantity, which is perhaps owing to the existing antagonism in the excretion of potassa and soda, shown by *Boecker* and *Reinson*, and more recently by *Bunge*. It is furthermore known that in febrile diseases the coloring matter of the urine considerably augments in quantity, which, according to *Vogel*, amounts to even more than four times the quantity excreted by healthy individuals on an ordinary full diet. No final product is augmented in the same measure as the urea, coloring matter of the urine, and the potassa, not even the phosphoric acid; it is even doubtful, after the careful determinations made by *Rosenstein*, whether its excretion—in the urine—is much augmented under the influence of fever. As regards the excretion of sulphuric acid, the greater part of which is likewise derived from the combustion of albumen during the fever, nothing certain is known, probably because its secretion does not regularly and rapidly follow upon its formation.

Those nitrogenous tissues which are rich in potassa and hæmoglobin, the mother substance of the greater part of urea, are therefore, especially prone to disintegration, namely: The colored blood corpuscles first of all, and then the muscles, while the brain and spinal marrow, with the nervous tissues in general, though likewise rich in potassa, may be excluded, as they furnish no coloring matter of the urine, and also because the discharge of phosphoric acid is not augmented. Experience teaches besides, that the central parts of the nervous system are least affected by the febrile consumption, or by that caused by inanition. The fact, that it is the colored blood corpuscles which, first of all, suffer and disintegrate during the febrile process, is corroborated by the observations of *Koerber*, which showed that the decomposability of the hæmoglobin was increased in febrile diseases, and the statement of *Mannasseïn*, concerning the general diminution of the colored blood corpuscles in size during fever and with an elevated temperature. But if those corpuscles and the hæmoglobin are destroyed to a great extent; if, in consequence, the body becomes poorer in those elements which effect

the reception of the oxygen from the air and its conveyance to the tissues, and if other elements do not take charge of this work, then the activity of the processes of combustion in the body must necessarily decrease in the same measure for want of oxygen. The further statement of Mannasseïn, that blood corpuscles rich in oxygen, increase in size, as also when under the influence of certain anti-febrile remedies—quinine, etc.—is a further proof that the function of the colored blood corpuscles is lowered during the fever; that the latter appropriate less oxygen, rapidly decrease in size and disintegrate.

Accordingly, the organism cannot absorb as much oxygen, and in consequence cannot oxydize as much material of the body to its final products during fever, as it can without fever and under the same nutritive conditions.

If, now. the one final product, urea, is found in too large a quantity. already consuming a certain quantity of oxygen more than usual, it follows that the other final products, which require still more oxygen, must naturally be diminished in quantity; and from this, it again follows that the combustion of the non-nitrogenous constituents of the body—the fat—and, accordingly, also the formation of carbonic acid during fever, cannot be simply augmented. The increased destruction of the colored blood corpuscles, the carriers of oxygen, then, forms another cause for the granular and fatty disintegration of the tissues, taking place here in a manner similar to the effect of poisons which act by abstracting the oxygen. The conclusion, therefore, is that in the majority of febrile diseases of man, the body decomposes exclusively, or, at least, more than normally, nitrogenous material, *i. e.*, albumen, and in consequence becomes relatively richer in non-nitrogenous, *i. e.*, fat. Without oxydation, only water, increased in quantity, can be formed from the ultimate products of the exchange of matter—by synthesis and dishydration.

The quantity of urine in fever is usually in proportion to the supply of liquids, but its secretion is more unfavorable than in the normal condition, as a comparatively smaller portion of the received water is discharged by the urine than in the absence of fever, but otherwise under the same conditions. The quantity of the evaporated water is augmented during the fever, and

amounts to even a little more than that of the expired carbonic acid; therefore, the quantity of water lost by evaporation is comparatively large. In what proportion the whole loss of water stands to its formation during the fever—with the exception of extraordinary losses—can as yet not be determined. With a large supply of water some of it may, as in the normal condition, be retained. The variations in the weight of the body during fever chiefly depend upon these unstable relations between the supply and loss of water

In comparing the economy or exchange of matter during the febrile process, as above stated, with that taking place in an individual kept on a perfectly normal diet, Senator remarks that the only two substances of excretion, from which the exchange of of albumen and fat may be calculated, are urea and carbonic acid, and that the daily normal excretion of the former amounts from 25 to 30 grms., while that of the latter is from 700 to 800 grms. This, based upon the values of combustion as determined by *Frankland*—4,263 units of heat for 1 grm. albumen, and 9.1 units for 1 grm. fat—corresponds to an exchange of 74 to 93 grms. albumen and 193 to 240 grms. fat, with a formation of heat of 2072 to 2580 units. The fever patients upon whom the investigations relating to the excretion of urea and carbonic acid were made, rather belonged to those who in their ordinary normal condition show a low equivalent weight of nitrogen, and whose daily excretion of urea deviates perhaps little from 25 grms. If these individuals discharge, at least during the first days and with a high fever, 40 to 50 grms. in 24 hours, then this is, in the most favorable case, a surplus expenditure of 25 grms. at the utmost in comparison with their normal condition, or a surplus exchange of 74 grms. albumen at the highest rate. In supposing that this albumen were completely oxydized, as in the healthy condition, to form urea, $C\ O^2$ and $H\ O^2$, an augmentation of heat, equivalent to 315 units, would result, or more still, because during the fever more albumen is disintegrated than corresponds to the urea.

In corroboration of the statements and views of Senator, but more especially for their own intrinsic value, I will recite some of the more recent investigations regarding the exchange of

matter during fever and inanition, obtained by *Zuelzer*.* They are as follows: "1. The total sum of the nitrogenous excretions is augmented during the state of febrile excitement, and diminished during the state of depression—inanition, convalescence. 2. The relative quantities of phosphoric and sulphuric acid—in proportion to the nitrogen—in the urine during the state of fever and hunger—do not exceed those found in muscle and brain. 3. In proportion to the nitrogen, more sulphuric acid is excreted in the state of fever and inanition, and less during convalescence than is excreted with a meat diet. Accordingly, these two final products, arising from the disintegration of the albuminous substances, are excreted through the urine in a relatively larger quantity than in the normal condition. During convalescence, however, the urine also contains—in a larger quantity than during inanition—nitrogenous substances, not derived from disintegrated flesh, but from the nervous substance, that is, from a tissue, in which the nitrogen is not associated with sulphur. Besides, the albuminous substances supplied for the reconstruction of the wasted constituents of the body, are mostly used in the body itself, while the secretion of bile is simultaneously augmented. 4. The relative quantity of the phosphoric acid is less during the fever than with a meat diet; during convalescence and inanition, however, it is larger, though smaller than on feeding with brain. During the fever, therefore, and simultaneous with the augmented disintegration of the nitrogenous tissues, phosphoric acid is retained in the organism to be excreted after the disappearance of the fever. In inanition—together with the diminished disintegration of the nitrogenous constituents of the body—the relative quantity of phosphoric acid in the urine is augmented. 5. Accordingly, the exchange of muscular substance, is augmented during the fever, whilst in inanition, as in convalescence, the exchange affects more the nervous tissue, which, in virtue of its richness in lecithin and cephalin (Thudichum) furnishes comparatively less nitrogen, but more phosphoric acid. 6. These processes in the nervous substance cannot be referred to a simple increase or decrease, as, during the state of inanition, according to the law of *Voit* concerning the loss of tissue during

***Virchow u. Hirsch*, Jahresbericht fuer das Jahr, 1877, Vol. I., p. 220.

the state of hunger, the total mass of nervous substance experiences the least loss. The regular change from retention to augmented secretion of the phosphates under existing and depressing influences, as also the widely varying results of the elementary analysis of the brain, rather indicate that the quality of the constituents of the tissues may experience rapid and intense changes."

The elevated temperature of the body in fever has usually been attributed to the increased disintegration or waste of tissue taking place during that process and liberating a surplus quantity of heat. The more recent investigations, cited above, however, have shown that the heat developed from this surplus exchange of matter is not sufficient to account for that discharged from the surface of the patient, and that there must be other sources besides. The investigations of Leyden and Senator, particularly, have furthermore demonstrated that the discharge of heat during the whole course of the fever, though augmented, is nevertheless subject to considerable variations. The quantity of heat stands in no fixed proportion with the temperature of those accessible parts of the body, upon which it is usually measured, but may be less with a high temperature than with a lower, and even sink to the normal standard; in the stage of defervesence, especially when a critical sweat occurs, the discharge of heat is highest, amounting to double and triple the normal quantity. During the hot stage, it is augmented to one and a half, or nearly double the normal amount.

In order to understand these variations existing between the formation and discharge of heat, we need only examine the particular mode in which the healthy organism regulates these processes in keeping up the equilibrium of heat. As the heat, derived from the exchange of matter constantly occurring in every tissue of the body, is distributed throughout the latter by the circulating blood, it follows that the richer any part or organ is in blood, the higher will be its temperature; but as the amount of blood which an organ contains is proportionate to the number and caliber of its minute blood-vessels, the arterioles, venules and capillaries, its temperature will change with the contraction or dilatation of these vessels. In the normal condition, the tonus of

these vessels, especially that of the arterioles possessing muscular fibers, is kept up by nerves—vaso-motor—connected with certain nerve-centers, chiefly placed in the middle portion of the medulla oblongata, but also in the spinal marrow; it is these centers, therefore, that regulate the normal temperature of the body by the amount of contraction or relaxation which they impose upon the muscular fibers in the walls of the vessels, or, in other words, by the amount of blood which they suffer to pass through the organ. The whole apparatus is reflex in its nature, and set and kept in operation by the impressions made, particularly upon the external surface of the skin; and it is thus that the application of cold will contract the minute vessels of the latter, while moderate heat will cause them to become relaxed. To a certain extent, however, the discharge of heat from the body is also regulated by the lungs, the respirations increasing or diminishing in frequency; this is especially the case in animals clothed with a fur. Even in the normal condition, the quantity of heat produced within the body is not always the same, as, for instance, during the process of digestion, when by the more extended decombination and combination of matter taking place, a surplus of heat is produced; or, also, during muscular exercise, when more muscular substance is disintegrated than in a condition of quietude and repose. With man, the limits of this capacity of regulating the temperature in the interior of the body are quite narrow, lying between 27°–37° C. of the surrounding air; whatever is required beyond he has to replace by accessory means, as clothes, etc.

Now, as regards the discharge of heat during the febrile process, it is not augmented in the beginning or cold stage, but rather diminished; in the hot stage, or at the height of the fever, however, it is augmented 70–75 per cent. in the average during the day, and still more at the critical defervescence. As in the normal condition, the most heat is lost during the hot stage by conduction and radiation, while at the critical defervescence the discharge takes place by evaporation.

It has already been remarked that the augmented exchange of matter, indicated by the final products, urea and carbonic acid, does not account for the surplus of heat present in the body dur-

ing the fever, and that there must be some other sources of heat besides. The most prominent of the latter are, according to Senator: 1. The consumption of those static forces, which, in the healthy organism, are stored up for the performance of any work. 2. The accumulation of heat during the pyrogenetic or cold stage of the fever. Besides these, other sources for the increased formation of heat may be sought in the greater disintegration and metamorphosis of albumen into urea, and in unknown processes concerning the formation of water.

With regard to the first of these sources, Senator presumes that the healthy body is in possession of latent forces, which are not generally liberated, but kept in store for extraordinary opportunities, such as an interrupted supply of nutriment, when they may be used, both for the performance of mechanical work, or for the development of heat. But as during the fever no external work of any import is done, these static forces are used up in the form of heat. Instead that in the healthy condition they are by the excitation of the will converted into mechanical work and heat, they will, on the other hand, under the influence of the febrile cause, be converted into heat only.

In the consumption of these static forces, which may either take place rapidly by mechanical work, or more slowly by hunger, carbonic acid is developed by the combustion of certain non-nitrogenous substances, containing these forces. The same should be the case, if the consumption of the latter takes place during the fever, to form a source for an augmented formation of carbonic acid during this process. When, nevertheless, such a source cannot be proved, or is not very conspicuous, even if present, no objection can be raised against the presumption that these static forces are liberated. For the surplus of carbonic acid formed here may be counterbalanced on the other side by being formed in a smaller quantity in such a manner that the albumen is not, as in the normal condition, completely consumed, but that it leaves behind, after the splitting off of the urea, a non-nitrogenous rest, more or less related to fat—the fatty degeneration of the parenchymæ in severe febrile diseases corroborates this hypothesis. The difference between the exchange of matter in a healthy and in a fevered individual is as follows: The healthy

individual converts, under ordinary conditions, daily, a certain quantity of albumen and fat into the corresponding quantity of urea and carbonic acid, and replaces the loss by an equal quantity of fresh supply, keeping thus his store of static forces at the same level. If the fresh supply is insufficient, that is, during a more or less perfect state of hunger, then he consumes, in proportion to his state of nutrition, a quantity of albumen and fat of his body, and his store of static forces decreases. But the combustion is always perfect, that is, the quantity of albumen and fat destined to the exchange is completely converted into urea, carbonic acid and water. During work, he consumes the same quantity of albumen, with the only difference, that the static forces, which during the state of hunger are more gradually consumed, are here liberated in a short time, giving rise to a rapid development of carbonic acid, which otherwise would have been discharged very gradually. During the fever, a larger quantity of albumen is disintegrated as during inanition, but only to urea and fat. The static forces are, perhaps in consequence of the enormous destruction of albumen, more rapidly consumed, and, for this reason, more heat and carbonic acid result in an equal time from this consumption than in a state of hunger; the carbonic acid, however, which would have resulted from the complete combustion of the albumen, is left out, so that, on the whole, nothing, or only very little more than in the corresponding time of hunger, is formed.

As regards the accumulation of heat during the cold stage, it is presumed that it really occurs. Even the normal discharge of heat during this stage would result in a saving or accumulation of it, because the changes in the exchange of matter are already taking place previously to the commencement of the chill, and as conditions for an augmented formation of heat may be found, besides, in the phenomena accompanying the chill itself. This presumption is moreover corroborated by the commencing augmentation of the discharge of urea, and the already preceding sensation of weakness and depression—phenomena which most probably depend upon the augmentation of the disintegration of albumen just beginning, and the consumption of the static forces in store. The spasmodic contraction of the blood vessels of the

skin, together with that of the smooth muscular fibers, causing the "goose skin," and even of voluntary muscles—causing the chattering of the teeth,—must give rise to a development of heat. In the beginning of febrile diseases, there is always a period to be found in which the morbid changes, the elevation of the interior temperature, the augmented secretion of urea and other changes in the urine, the increased frequency of the pulse and of respiration, and, finally, various subjeetive sufferings, show the existenee of the febrile process, and with it the augmented formation of heat, even in the absence of the normal heat of the skin, or without an augmentation in its discharge; a period, therefore, in which an accumulation of heat may be presumed to take plaee.

The variations in the quantity of heat discharged, occurring during the fever, do not depend upon a total loss of the capacity of the skin to regulate the temperature of the body, but are rather owing to an abnormal excitability and irritation of the cutaneous vessels, brought about by the influence of the original cause of the fever, and probably reflected to the respective nerve-centers. It is the irregular and unequal eontraetion of these vessels, therefore, which prevent the equalization of the surplus of heat present. This irregularity of contraction and dilatation of these vessels during the febrile process has been satisfactorily proved by Senator and other investigators, who carefully observed it on the vessels of the ears of fevered rabbits and dogs; and it explains the alternate sensations of heat and eold, experienced by fever patients, especially before the fever is completely established.

From the above statements, concerning the elevation of temperature during the febrile process, it may be coneluded that it is brought about by a disproportion between the abnormally augmented formation and diseharge of heat; though the discharge at the height of the fever may be greater than normal, and at times even greater than the febrile formation of heat. The disproportion, therefore, is not equally prominent in each phase of the fever, and it is supposed that every hot stage has been preceded by a pyrogenetic, or cold stage, for the accumulation of the heat, just as, on the other hand, it terminates by a stage of defervescence with an augmented discharge of heat. In mild

cases of fever, the same variations occur in the discharge of heat, only more gradually and less intense.

Of late years, numerous additional investigations, regarding the febrile process have been made, chiefly for the purpose of determining the exact relation existing between the central and peripheral temperature, and, also, of the relative temperature of different parts of the external surface of the body itself, as, for instance, that of the right or left side of the thorax during febrile diseases of the respiratory organs. In these investigations, the temperature of the axilla, or, in some instances, of the rectum, was taken as a standard of the internal heat, while the skin between the toes, or other parts of the surface were chosen for measuring the external temperature. But, though the results of these investigations, in general, corroborated the statements of Senator, and with it the neuro-pathological theory of Virchow, some contradictory statements have not been wanting. Thus, *Murri*,* basing his views upon the results of numerous experiments on animals, denied any dependence of the febrile process from the nervous system as chief regulator of the animal heat, and attempted to establish a bio-chemical hypothesis of fever in place of the neuro-pathological, now prevailing. He especially asserted that, in most cases of fever, no abnormal proportion between the peripheral and central temperature could be shown, and that the difference beween these temperatures were neither more variable, nor much greater than in the normal condition; but, on the contrary, often, and for a long time, remained unchanged during the course of the disease; frequently, even. the surface would be warmer than the central organs. *Jacobson*,† who experimented on a number of fever cases of pericarditis, pleuritis, typhoid fever, pneumonia, articular rheumatism, and tertiary intermittent fever, made use of a thermo-electrical apparatus. For the determination of the peripheral temperature, he introduced electrodes, in the form of fine needles, beneath the upper layer of the epidermis upon different parts of the cutaneous surface; for the central temperature the axilla was chosen. The results of these examinations were very inconstant. While, at

* L. c. für das Jahr 1875, Vol. I, p. 281.
† L. c.

one time, the difference of temperature between the axilla and the upper layers of the cutis was less during the fever than during the apyrexia, it would be greater at other times. Thus it varied irregularly between different places of the skin in the same individual, for, while the thermometer showed one and the same degree of temperature in the axilla, that of the skin was observed to undergo very considerable variations. The difference between the central and peripheral temperature was found to be in no way less than during the apyrexia. The same results were obtained in measuring the comparative temperature of the mouth and skin. These observations showed that at the acme of the hot stage, also, an alternate contraction and dilatation of the cutaneous blood-vessels takes place, and that during this stage, the quantity of blood in these vessels at the periphery of the body, and, in consequence, also the discharge of heat, are subject to variations within extended limits not only at different times, but simultaneously on different places. *Schuelein*,* with the view of answering the same question, instituted a series of thermometrical examinations on fever patients, for which he had availed himself of maximal thermometers with very small cylinders, corresponding very accurately with each other, and of which the one was introduced in the closed axilla, while the other was put between the first and second toe in such a manner as to completely embrace the bulb containing the mercury. The patients were quietly lying in bed under a light cover; the temperature of the room was almost always the same, varying with some exceptions, between 18.0° and 20.0° C. In healthy individuals, it was found that while the temperature of the axilla remained nearly constant, that between the toes showed great variations. In the course of typhoid fever, peritonitis, acute articular rheumatism, erysipelas, endometritis, miliary tuberculosis, and cheesy pneumonia, continuous variations of temperature of the skin, not corresponding with those of the axilla, took place. In typhoid fever, they were observed within considerably wide limits, even when measured every quarter of an hour. During a severe frost a descent of the temperature of the skin nearly coincided with a rise of that in the axilla. Another series of observations, the

* L. c.

results of which corroborated the statements of Jacobson and Schuelein, were made by *Schuck*.* *Wegscheider*,† who made his examinations on pneumonia and typhous patients, states, that the temperature of the periphery was subject to great variations, not running in any way parallel with those of the axilla. They were greater during the fever than in the feverless condition, a fact which he regards as depending upon an abnormal state of excitation of the cutaneous vessels.

A number of other observations have been made on this subject, which it is needless to cite, as they likewise corroborate the variations occurring in the contraction and dilatation of the cutaneous vessels during the febrile process.

In reviewing the preceding sketch of the febrile process, it will be found that though the chemical and physical processes concerned were satisfactorily explained, nothing was said which could throw any light upon the primary cause inducing the abnormal phenomena characteristic of fever. But as, in order to form a correct idea of the general pathology of yellow fever, it is important to have a clear understanding, not only of the chemical and physical processes concerned in the febrile process in general, but also of the principal views which at the present time are entertained as to its primary cause, a brief discussion on the subject is demanded.

Judging from what is known about the chemistry and physics of the febrile process, as demonstrated in the preceding sketch, the most prominent phenomenon of the whole is the over-production of heat, depending chiefly, but not entirely, upon an increased disintegration and exchange of matter. This heat, however, though its formation may from the beginning of the fever be going on at an equal rate, is not equally distributed throughout and discharged from the body. In consequence, the elevated temperature in fever, as once said before, is brought about by a disproportion between the abnormally augmented formation and the not in the same degree augmented discharge of heat, though the discharge at the height of the fever may be greater than normal, and at times even greater than the febrile

* L. c. für das Jahr 1877, Vol. I, p. 219.

† L. c.

formation of it. But, while the chief cause of the latter is the augmented disintegration and exchange of matter, the cause of the unequal discharge of heat, depending upon an abnormal and irregular contraction of the cutaneous blood-vessels, must be looked for in the nervous system. The question to be answered in relation to the primary cause of fever, therefore, is whether the increased waste of matter in the organism is the result of the accumulation of the normal quantity of heat within the body, depending upon the diminished discharge from the surface, on account of the irregular and abnormal contraction of the blood-vessels of the skin,—or whether the augmented disintegration of matter, especially the albumen, preceded the contraction of these vessels, and by some irritative influence upon the respective nerve-centers had perhaps, itself, been the cause of the contraction. In the one case, the process would have commenced in the nervous system, and be in concert with the neuro-pathological theory; in the other, its starting point would have been the blood, and it would correspond to the principles of humoral pathology. In examining the subject a little closer, it will be found that neither the one nor the other theory can be strictly and exclusively applied to every form of fever. For, in taking, for example, the febrile process as it accompanies the so-called infectious diseases which are supposed to depend upon a certain poisonous material entering the blood through the avenues of the lungs and the alimentary canal, it will be obvious that the process commences in the domains of humoral pathology; while, on the other hand, the febrile process following the shock of a severe bodily injury, and representing the so-called symptomatic fever, most probably took its start from the nervous system. Therefore, the primary cause of some fevers will be strictly humoral, whilst that of others will be nervous. But it must be remembered, that though in a number of fevers the effect of the cause, representing some noxious matter, is directly made upon the blood, it may also, through the medium of this liquid, very rapidly extend to the nervous system, which, reacting upon the one or other organ of the body, may induce serious pathological changes. And, in the reverse, in those fevers associated with severe surgical injuries, the disturbance and derangement in the nutrition of

the injured parts may give rise to a certain pathological condition of the blood, which, through the medium of the nervous system, may conjure up the febrile process. We see, therefore, that the febrile process in general cannot be made exclusively to fit one or the other theory, but being of a complex nature, remains independent. .

The neuro-pathological theory of *Virchow*, applied to the febrile process, explains many of the phenomena manifested, as, for instance, that of the irregular discharge of heat from the cutaneous surface by an irregular spasmodic contraction and dilatation of the cutaneous blood vessels, caused by a morbid irritation of the vaso-motor nerves. But, although the phenomenon of the non-equalization of heat is of a nervous origin, it does not necessarily follow that the augmented disintegration and exchange of matter is likewise the direct result of a perverted nervous action, for it has, as yet, not been positively shown that the original production of animal heat depends solely upon the nervous system, unless we presume the existence of special nerve-centers performing the function of regulating the exchange of matter, and with it the production of heat. The experiments of *Magendie*, *Bernard*, *Buettner*, *Rollet*, *Mantigazza*, *Schiff*, *Vulpian*, *Obolensky*, *Haidenhain* and *Legros*, made on animals in relation to this subject, and the clinical observations of *Samuel*, *Weir*, *Mitchell*, *Morehouse*, *Keen*, *Charcot*, *Erb*, and others, on man, however, seem to indicate the existence of so-called " trophic " nerve centers, which regulate the nutrition of the tissues and organs, though on the other hand, a number of other investigators have obtained negative results from their experiments. The decrease of heat in paralyzed limbs, also, points to the influence of the nervous system upon the exchange of matter in the paralyzed parts. A number of experiments, consisting in the section of the spinal marrow, have likewise been made on animals by *Bezots*, *Ludwig*, *Thiry*, *Tscheschichin*, *Schiff*, and others, for the purpose of determining the variations of temperature in the extremities, with other observations on cases of severe injuries of the spinal marrow of man ; these, however, may be passed over, as the results obtained are to a certain extent contradictory, and

only seem to indicate local disturbances in the function of the blood vessels.

Now, even in recognizing the doctrine of trophic nerve-centers and nerves, and in admitting that the exchange of matter in the organism, constantly taking place in the fluids and solids, depend upon nervous stimuli, a special cause will still be required to act as such, and, accordingly, it may be presumed that in a similar manner as the nerve-centers presiding over the circulatory and respiratory functions, are stimulated to their rythmical reflex actions by the relative quantity of oxygen and carbonic acid in the blood, the normal combinations and decombinations of matter, constantly taking place in the blood and tissues, may form a stimulus for the trophic centers. As long as the organism remains undisturbed by external injuries, or by the influence of noxious substances, introduced into the blood from without, the trophic centers, then, will discharge their function in the same regular reflex manner as the respiratory; the exchanges of matter will take place in their just proportion, *i. e.*, each atom of matter will be replaced by an atom of fresh matter, and the normal nutrition of the tissue will be preserved. At the same time, the quantity of heat liberated by the exchange of matter will be counter-balanced by an equal discharge, regulated by the normal contraction and dilatation of the cutaneous vessels. But, as soon as any foreign substance, that is, a body incapable of being assimilated by the organism for the rejuvenation of the tissues, and therefore incapable of becoming a constituent of the latter, enters the blood, it will be removed by one or the other of the secretory organs, the only outlets from the organism. There are a large number of substances, some of which are used as medicines, which thus may enter and leave the organism without injury, and be detected in the secretion, while there are others, which, after entering, will, either catalytically, or by entering into combination with the organic constituents of the blood and tissues, exert a noxious or fatal influence upon it. To these belong the so-called infectious poisons with which we have to deal in this treatise.

In the symptomatic fevers, the morbid impression may be carried to the vaso-motor or trophic nerve-centers by the sensory

nerves of the skin, or of the traumatic lesion, affecting them in the same manner as the respiratory centers are affected by sudden impressions made upon the skin, etc.; in the fever of infectious diseases, however, experience teaches that they are affected through the medium of the blood. Even Virchow, when founding the neuro-pathological theory, admitted this probability in saying:* "The rapidity with which febrile phenomena appear and disappear, likewise points to a cause residing in the nervous system, though the noxious material, affecting the nervous system, may be sought in the blood." And, further on: "In the study of the chemical nutritive processes of the body, it is of advantage to exclude the nerves as long as possible, as it has been shown that they exert no other influence, but in determining quantity or, acting as excitors or moderators, for all qualitative changes come from other directions."

In studying the general pathology of yellow fever, we must keep in mind that the clinical phenomena exhibited during its course, and the pathological changes met with after death, *do not*, as I have hinted at before, *exclusively* belong to this disease, but are equally observed, though in a more or less modified form, in other infectious, and even non-infectious diseases. It is only when they are considered as a totality, that they may represent the characteristic features of the disease. Thus, the continuous type of the febrile process witnessed in yellow fever, together with the congestion and parenchymatous infiltration and degeneration in various organs, are equally observed in other infectious diseases, particularly those of a contagious nature. The chief difference seems to lie in the specificity of the noxious poison, and in its tendency to affect particular organs in the different diseases, while its general effects upon the whole organism in these affections bear much resemblance to each other.

In the beginning of this treatise, I have already remarked that, in all cases of yellow fever, as well as of other infectious diseases, there is a prodromal stage, during which the poison exerts its noxious influence upon the blood, and primarily deranges the normal exchanges of matter. The symptoms of this stage, consisting, as we have seen, in a general discomfort, anorexia, lassi-

* *Virchow.*—Handbuch der Speziellen Pathologie und Therapie, 1854, Vol. I, p. 36.

tude, headache, etc., are decidedly nervous in character, from which fact it may be presumed that it is the nervous apparatus, which, first of all others, experiences the effects of the noxious poison. Now, although it is the blood with which the poison comes first into contact, it remains nevertheless difficult to determine whether it is directly carried by this fluid to the tissues of the nervous apparatus to make a direct impression upon them, or whether, in one way or other, it first contaminates the plasma of the blood, and, accordingly, makes an indirect impression upon the protoplasm of these tissues by deranging their normal nutrition. The latter supposition appears to be the most probable. At any rate, the influence which the poison at this period of the disease exerts upon the nervous system, is depressive in its nature, and appears to be directed to the vaso-motor centers. The immediate effect of a depression of these centers is a relaxation of the muscular elements in the walls of the blood vessels, especially of the smaller arteries, followed by a dilatation of these vessels and a hyperæmic condition of a moderate degree, upon which the prodromal phenomena seem to depend. Judging from the degree of the headache, it appears that the hyperæmia of the brain, upon which it depends, is at this period principally confined to the pia-mater, though the minute vessels of the cortex cerebri, also, may be slightly over-filled with blood. The sympathetic ganglia likewise suffer from the effects of the poison, and, moreover, exert their depressing influence upon the functions of the liver, stomach and kidneys. The degree of the prodromal symptoms in the different cases, is obviously proportionate to the quantity and intensity of the poison absorbed, but also to the particular susceptibility to the noxious influence of the poison by the person infected. In persons very susceptible to the absorption and influence of the poison, and who are exposed to it in its intense form by proximity to a severe case of yellow fever, the prodromal stage, therefore, may be comparatively short, while in others, not as susceptible, and exposed to the poison in a milder form, the prodromal phenomena may be milder, and extended over a longer period of time. From this difference observed in the severity and length of the prodromal stage in different cases, we may presume that the abnormal disintegration and exchange

of matter in the organism, resulting from the effects of the poison, must have proceeded to a certain extent, before the febrile process can start into action. The augmented quantity of urea, found in the urine before an elevation of the normal temperature of the body can be perceived, shows the correctness of this supposition. But, while the first impression of the poison upon the nervous system is of a depressive character, a sudden change takes place with the true commencement of the febrile process, evidently owing to a certain reactive effort of the vaso-motor nerve-centers, and manifesting itself in the abnormal excitability and irritation of the cutaneous blood vessels. It is impossible to decide whether this irritation proceeds from the vaso-motor nerves of these vessels, or from the sensory nerves of the skin, to be propagated to their respective nerve-centers, thus constituting a simple reflex action; or, whether it originates in the latter themselves, and is originally caused by the now concentrated effects of the infectious poison, or by the products arising from the augmented disintegration of albuminous substances, accumulated within the blood, and increasing the previously commenced disturbance of nutrition. The first effect of the augmented excitability of the vaso-motor nervous apparatus, then, is observed in the contraction of the cutaneous blood vessels, giving rise to the phenomena of the pyro-genetic stage, the mildness, severity, or duration of which evidently depends upon the quantity and intensity of the fever poison in the blood. Although those initiatory symptoms of the febrile process are subject to great variations in different cases of the disease, I do not think that they are ever entirely absent, but that, even in those cases in which no regular chill is observed, an alternate sensation of cold and heat, indicating the irritation of the respective nerve-centers, is experienced by the patient,—while in others, in which a regular chill, or even rigor, occurs, the spasmodic contraction of these blood vessels is more decidedly pronounced. As soon as the nervous energy, causing the contraction, is exhausted, a relaxation of the muscular fibers in the walls of the blood-vessels, followed by a dilatation, takes place, and in consequence of a larger quantity of blood coming from the central and warmer parts of the body, passing

flow through the vessels, the temperature of the skin gradually rises, until the hot stage of the fever is fully established.

In considering the disturbance of the nervous functions in yellow fever, we must not imagine that a depression or excitation of the nervous tissues takes place simultaneously throughout all parts of the nervous system, and that in consequence the blood vessels of all organs must be in a corresponding state of dilatation or contraction. On the contrary, as will be seen, the vessels of one part of the body may be relaxed, while those of another may have preserved their normal tonus, or, as in the case of the cutaneous vessels, may alternately be contracted or relaxed. In order to appreciate correctly the relative disturbances in the functions of the various organs of the body, and the pathological changes taking place in the blood and tissues during the whole course of an infectious disease like yellow fever, one should be familiar with all the anatomical and physiological minute details of the entire organism, the study of which, alas! is rather neglected by the majority of practicing physicians. Without the knowledge of these details, which, after all, constitute the basis and greater portion of true medical science, the physician can only form an indefinite, vague idea of the normal and pathological processes taking place in the human organism, while, with it, he may represent to his mind the entire mechanism of the body in all its details, and in full operation.

Already, before the commencement of the hot stage, pains in the joints and limbs, as we have seen, are added to those in the head, increasing in severity with the rise of the temperature, until the fever is fully established, when they either disappear, or continue in a milder form during the hot stage. These pains, which are most severe in the lumbar region and pelvis, must probably depend, as mentioned once before, upon the congested condition of the blood vessels of the pia mater, and of the spinal marrow in the lumbar region, whence they are reflected to the joints and muscles affected. Whether these pains, as well as those in the head, are simply owing to the pressure of the congested blood vessels upon the nervous substance, or whether their severity partially depends upon the direct noxious influence of the infectious poison upon the nervous tissue of the affected parts,

I will not venture to decide, though the latter supposition appears probable from the fact, that, in fatal cases, these pains generally disappear before death, while the blood vessels are still found congested with blood corpuscles after death.

The nervous apparatus, through the influence of which the circulation of the blood is sustained and regulated, is quite complex, and consists of several nerve-centers. While the rythmical movements of the heart, by which the blood is kept in circulation, are most probably caused by the influence of certain nervous ganglia situated in the muscular substance of the heart itself, they are regulated by other centers situated in the medulla oblongata, and operating through the pneumogastric and sympathetic nerves; the nerves which the heart receives from the cardiac plexus are derived from these sources. The fibers of these nerves, however, differ very considerably in their function, for while the pneumogastric fibers transmit only inhibitory stimuli, the other transmit stimuli which accelerate the heart's action. Accordingly, an irritation of the fibers of the pneumogastric nerves will be followed by a retardation, or even arrest of the movements of this organ, while an irritation of the centers in the medulla oblongata will produce an acceleration, as long as their communication with the heart through the spinal marrow, rami communicantes, first thoracic ganglion, etc., is not interrupted. An acceleration of the heart's action will also be produced by an increased pressure of the blood within the cavities of the organ, as may be caused, for example, by a contraction of the smaller arteries, depending upon an irritation of the vaso-motor centers, likewise situated in the medulla oblongata. From this it is easy to understand how an irritation of the medulla oblongata, produced by the noxious influence of the yellow-fever poison, will give rise to one of the most prominent phenomena of the febrile process, the frequency of the pulse. Besides this, the elevation of temperature also, depending upon the augmented disintegration and exchange of matter, initiating the febrile process, forms another cause for the accelerated action of the heart. The latter assertion, however, must appear contradictory to the circumstances, before mentioned, of the falling of the pulse on the second day, a time when the temperature is still rising. But may not this phenomenon be

owing to an irritation of the inhibitory centers of the pneumogastric nerves, set up at this time?

The abnormally augmented disintegration and exchanges of matter in the organism, originally caused by the presence of the infectious poison in the blood, and giving rise to an increased formation of urea and other products, as well as to an augmented quantity of heat, will now continue, until the poison is destroyed, or eliminated from the system, while, at the same time the products arising from these abnormal processes, or the direct action of the poison itself upon the nervous tissues, or upon the morphological elements of the blood, may give rise to the abnormal excitability and irritation of the involved nerve-centers with their nerves.

The morbid excitability of the nervous tissues, however, does not appear to be confined to the centers and nerves already mentioned, but, moreover, extends to other parts of the nervous system, giving rise to other phenomena of the hot stage, consisting in the congestion and deranged secretion of several organs. Thus, the congestion of the blood vessels of the conjunctiva very likely depends upon a neuro-paralysis of the vaso-motor nerves, and is similar in character, though inferior in degree, to that produced in the blood vessels of the rabbit's ear by the well known experiments of Claude Bernard of dividing the sympathetic nerve in the cervical region. The deeper seated pains of the eye, and also the slight photophobia, are phenomena which depend upon the irritation of the trigeminal nerves and their centers. In the same manner, the congestion and irritation of the mucous membrane of the pharynx, œsophagus, and stomach are explained; for in considering the fact that all the minute blood vessels of the brain, but particularly those of the pons varolii, corpora quadrigemina, and medulla oblongata, are found after death in a congested condition, completely filled with blood corpuscles, there will be no difficulty in understanding the congestion and irritation of these mucous membranes, if we remember that the nuclei, or centers, of the trigeminal, glosso-pharyngeal and pneumogastric nerves, supplying these parts, are situated near each other, alongside of the aqueduct of Sylvius and the floor of the fourth ventricle of the brain, and that all these nerves closely communi-

cate with the sympathetic. Judging from the scarlet-red color of the congested vessels of the conjunctiva, gums and edges of the tongue, during the first part of the hot stage, the congestion is arterial in its nature, that is, depending upon a relaxation of the arterioles and the ensuing afflux of blood. As regards the stomach, it hardly needs mentioning that the nausea and inclination to vomiting are due to the irritation of its mucous membrane, the secretory function of which, however, is not suspended, but only deranged, as shown by the quantity of frothy mucoid liquid thrown up at this time. As regards the liver, kidneys and supra-renal bodies, I have already mentioned, when discussing the pathological anatomy of these organs, that the parenchymatous degenerations, observed after death, have been initiated by a congestion of the blood vessels, depending most probably upon the same causes as that of the mucous membranes above discussed. But, before passing to the discussion of these parenchymatous changes, I must make some remarks on the condition of the blood.

In the section of this treatise devoted to the pathological anatomy of the blood and a number of organs, I showed that, besides an unusual tendency of assuming the mulberry or thorn-apple forms, manifested by the colored blood corpuscles, nothing abnormal, or foreign, could be detected in this fluid, when carefully examined directly after it had been removed from the living patient; while, on the other hand, in almost every organ in which a congestion had occurred, numerous extravasations or infiltrations of the coloring matter of the blood corpuscles, the hæmoglobin, into the parenchyma were met with. The question arises, therefore, whether the hæmoglobin parted from the colored blood corpuscles only in those places where the extravasations occurred, by virtue of the existing retardation of the circulation in the congested capillary vessels, or whether it escaped from the corpuscles while they were still in an active circulation. In answering this question, it may be said, that the direct cause of these extravasations evidently was the retarded circulation, but that there also existed a remote cause, consisting in a want of coherence between the hæmoglobin and the protoplasm of the blood corpuscles, facilitating, as soon as the retardation took place, the

escape of the former from the latter. And, it may further be presumed, that not all the hæmoglobin escaping from the blood corpuscles, passed through the walls of the vessels, but that perhaps the greater portion became mixed with the liquor sanguinis and was carried into the general circulation, giving rise to the jaundice. Thus, it will be seen, *that the icterus in yellow fever is not owing to the presenee of bile in the blood*, as is believed by a large number of physicians, *but to the presence of free hæmoglobin*, and represents in truth the so-called "*hematogenous*" jaundice. A "*hepatogenous*" jaundice cannot take place, as the larger as well as the smaller hepatic ducts are found perfectly open, and as the secretion of bile during the disease, in the majority of cases, is rather diminished, or even suspended.

As regards the presence of free hæmoglobin in the blood, however, some doubt might still be expressed on account of its not having been demonstrated by the microscopical examination of so many specimens of fresh blood, taken from the living patients. The reason for this failure is, that the quantity of hæmoglobin contained in the exceedingly thin layer of blood required by microscopical examination, is too small to exhibit its yellow color to the eye of the observer, and that in order to be seen, the blood should be saturated with the coloring material to such a degree as would require a quantity larger than would be consistent with life. Free hæmoglobin, therefore, may be present in the circulating blood without being detected by the microscope. The faintly yellowish tint, appearing, in a number of cases, as early as the third day of the disease, in the conjunctiva and the skin, corroborates this assertion ; though, in the majority of cases, the jaundice appears later, if it appears at all during life. The yellowish tint of the conjunctiva and skin, however, is not produced by the free hæmoglobin still contained in the circulating blood, as its presence is not perceived until it has escaped from this fluid into the juices of the surrounding tissues, to be absorbed by the cells of the epithelium of the conjunctiva, or those forming the lowermost stratum of the epidermis of the skin.

The extravasations of hæmoglobin into the parenchyma of various organs, which I have observed to occur in yellow fever, fully corroborate the generally accepted fact mentioned before,

that in the febrile process, it is these nitrogenous tissues, rich in potassa and hæmoglobin, especially the colored blood corpuscles and muscles, which are most prone to disintegration, and which first suffer from the effect of the poison.

Let us now direct our attention to the liver. Although in most cases of yellow fever, as I have shown, the traces of congestion of the blood vessels, observed after death in this organ, are not as conspicuous as in other organs, there remains for the reason already given, no doubt but that the liver is one of the first organs which experience the deleterious effects of the poison, and participates in the general hyperæmia resulting from the depression of the vaso-motor nerves, manifested during the prodromal stage. But, like in the stomach, as soon as reaction takes place, the secretion of bile is resumed, and, very likely, for a short time abormally increased, as may be inferred from the vomiting of bilious matters, observed in a number of cases during the commencement of the disease. Judging from the fact that most cases of miasmatic fevers, even the simple intermittent, are accompanied by some derangement of the biliary functions, I have always been inclined to regard the liver as that organ through which the organism makes the first attempt at eliminating the miasmatic poison by stimulating its secretory function. The same may take place in yellow fever, as above mentioned, though the abnormally stimulated secretory function will soon be exhausted, and an opposite condition prevail. But, besides this stimulation through the secretory nerves, it appears very probable that the liver receives another stimulus, proceeding from the part of the blood, for the purpose of removing, and converting into bilirubin, the free hæmoglobin escaped from the colored blood corpuscles. But like even in the normal condition, the amount of labor which the parenchyma of a gland can perform, stands in a certain proportion to the quantity or number of its secreting cells, only a small portion of the free hæmoglobin can be converted into bilirubin by the liver, while the rest extravasates through the capillaries of the different organs and tissues as we have seen, to be absorbed by the surrounding cells, or to mingle with the fluids of the tissues. Thus, the abnormal stimulation of this organ, accompanied by the increasing disturbances of the nutri-

tion of the whole organism, soon leads to a state of exhaustion. But, while these functional changes are taking place in the liver, the abnormal processes in the blood, relating to the augmented disintegration of the albuminous constitutents, and their metamorphosis into the final products urea, carbonic acid and water, are likewise running their course. The albumen, thus undergoing disintegration, may be derived from two sources, *i. e.*, from the circulating albumen of the blood, designated by *Voit* the "store albumen," or from the albumen of the tissues, the "stable" or "tissue-albumen." As the former, on account of the small quantity, is soon consumed, it is especially the latter which suffers the greatest losses during the febrile process. In consequence of the augmented formation of urea, consuming considerably more oxygen than is normal, the other final products, requiring still more oxygen for their formation, must fall short in quantity, and the combustion of the non-nitrogenous constituents be retarded. But, as an abnormal quantity of albumen is decomposed without a corresponding quantity of non-nitrogenous material, such as fat, the latter accumulates in the blood, and gives rise to the *fatty infiltration* of the different organs, already described.

Fatty infiltration of the liver, besides being met with in infectious diseases, also frequently occurs in chronic diseases accompanied by great exhaustion of the system, such as phthisis, chronic diarrhœa, dysentery, etc., in which the normal processes of nutrition and assimilation are severely deranged, so that a part of the albumen, destined for the rejuvenation of the tissues, instead of being appropriated for this purpose, becomes converted into fat; the same occurs through the imperfect combustion of the non-nitrogenous substances in the lungs. Generally, in these diseases, the nutrition becomes deranged only gradually, and, if fatty infiltration of the liver takes place, the process advances, in most instances, at the same slow rate of the original disease. In yellow fever, however, the case presents a different feature. Through the deleterious influence of the infectious poison, the disintegration of albumen and the exchanges of matter take place quite rapidly, and the fatty infiltration of the liver may commence at a comparatively early period of the disease, and, in

advancing, seriously interferes with the neighboring organs. For, besides the diminution and final suspension of the biliary secretion which it causes, it also interferes with the portal circulation by the pressure, which the abnormal amount of fat, deposited by the blood and absorbed by the hepatic cells, exerts upon the capillaries and inter-lobular vessels. And it is this pressure by which the congestion, representing the first stage of the pathological process in this organ, is gradually reduced. In advanced cases of fatty infiltration, therefore, the minute vessels are very rarely found over-filled with blood; on the contrary, the capillaries, as we have seen, are mostly found empty. The disturbance in the portal circulation, however, will soon be felt by the tributaries of the portal vein, for, while the passage of the blood through the liver is rendered more difficult, a congestion of these veins will be the result, which, in extending backward to the minute venules of the mucous membrane of the stomach and intestines, will give rise to that peculiar congestion of these organs, already described. In the stomach, this congestion is mostly accompanied by an infiltration of hæmoglobin into the surrounding tissues; and, in severe cases, ruptures of the minute venules, or capillaries, situated between the epithelial and glandular layers, will occur, and give rise to that much dreaded clinical phenomenon, known as "black vomit."

The vomiting of black matters in yellow fever has always been regarded as a most unfavorable symptom. The morphological elements of the blood which these matters contain are derived, as we have seen, from the minute hæmorrhages caused by the rupture of the vessels just mentioned. It is quite obvious that such a hæmorrhage must result in the direct relief of these minute vessels from their congested condition, and that the small quantity of blood, thus lost, is in itself inadequate to cause the fatal issue of the case, though *it most certainly indicates a very diseased condition of the liver, as well as a low state of the whole organism;* and it is, in this respect, that it becomes an important factor in the prognosis of the case. Besides this, although the primary congestion and irritation of the stomach is, during the first three days, rarely accompanied by much pain, when pressure is made upon the epigastrium,—it will finally, when aggravated by the

advancing fatty infiltration of the liver in the manner described, give rise to a sensation of dull pain and fullness in the organ, rendering pressure insupportable to the patient. The condition of the liver, and with it that of the whole organism, therefore, may be accurately diagnosed by that of the stomach, and will notify the physician of the approaching danger. Very rarely black vomit occurs before the fourth, or even fifth day; in most cases, perhaps, it takes place still later, at a time when the pathological changes in the various organs have attained a high degree, and when the nervous energy of the organism is nearly wasted, producing an almost complete depression and exhaustion of the patient.

If, after the elimination of the poison from the system, indicated by the cessation of the febrile process, the pathological changes of the parenchyma of the liver have not advanced to a very great extent; that is, if the protoplasm of the hepatic cells itself, has not undergone *true fatty degeneration*, and, if sufficient energy is left in the nervous organs to supply the wants of the organism—*black vomit may occur without proving fatal.* For, after the removal of the disturbing cause, the poison, the condition of the blood will gradually attain again its normal standard, the tissues will again be properly nourished, and, in consequence, the deposition of fatty matters into the parenchyma of the liver will cease, and, finally, the fat in the hepatic cells be reabsorbed by the blood. In this manner, quite a number of patients recover from black vomit. In fact, in most cases in which black vomit occurs, the patient feels relieved after the ejection of these matters, and imagines that he will get well. In children, especially, the occurrence of black vomit is not as often followed by a fatal issue as in adults. This is owing to the exchanges of matter, especially in those organs pertaining to organic life, being more active than in adult life; while, on the other hand, the organs of animal life, particularly those of the nervous system, are in children more impressible and sensitive.

In many fatal cases of yellow fever, especially those in which the third stage is protracted, the pathological changes of the liver do not remain confined to a simple *fatty infiltration*, but advance to a *true fatty degeneration* of the protoplasm of the

hepatic cells, as I have described in the section of pathological anatomy. These cases, of course, as may be expected, prove necessarily fatal.

The relationship existing between the stomach and the liver, also exists between the latter and the intestines, and it is therefore natural that the same pathological phenomena should be observed in these organs, though inferior in degree. Accordingly, in a number of cases, hæmorrhages, similar to black vomit, are observed to take place from the mucous membrane of the small intestines, which, mingling with the mucous matters, pass per anum, though, sometimes, the black matters from the stomach may also be voided in this direction.

The infiltration and degeneration of the liver, associated with congestion and minute hæmorrhages of the stomach—black vomit—are so constantly met with in every fatal case of yellow fever, that they may safely be regarded as a characteristic phenomenon of this disease. In cases in which the black matters are not ejected during life, they will, almost always, be found in the system after death.

In taking now a glance at the kidneys, the pathological changes of which have already been fully discussed in their appropriate place, we find that these changes have, as in those organs already discussed, been preceded by a hyperæmic condition primarily depending upon the same cause, that is, a partial paralysis, or paresis, of the vaso-motor nerves. One of the first phenomena, depending directly upon the relaxed condition of the minute vessels, especially the arterioles, is the albuminuria, making its appearance quite early, on the second or third day of the disease. It is now generally accepted that this phenomenon, very frequently accompanying even mere functional disorders of the kidneys, chiefly depends upon an increased pressure of the blood upon the inner surface of the walls of the minute vessels of the glomeruli, as has already been noted. In yellow fever, the conditions necessary to the production of albuminuria, are rendered especially favorable by the relaxed state of the smaller arteries, so that, soon after the commencement of the febrile process, when the heart's action is increased, albumen may make its appearance in the urine, without being accompanied by other products indica-

tive of organic changes in the organ. The degenerative processes commence at a later period, during the second stage of the disease, when the increased disintegration of albumen and exchange of matter, entailing a complete derangement of the nutrition of the various organs, has reached a higher degree. As in the liver, a slight reaction, resulting in a temporary stimulation of the secretory functions and following the general nervous depression, also takes place most probably in the kidneys. This stimulation may be caused by the accumulation of urea, or its components, in the blood, calling upon the kidneys for elimination from the organism. And it seems to be not impossible that this same cause, together with the deranged nutrition of the epithelial cells, lining the uriniferous tubules, may also give rise to that abnormal product of secretion of which the cylindrical infarctions are formed. The nature of this abnormal secretion, and the manner in which the different kinds of cylinders are formed, have already been so thoroughly discussed as to require no further remarks in this place.

It has already been mentioned that the degenerative changes in the parenchyma of the kidneys are not observed to have taken place in the same degree in all fatal cases of yellow fever, but, on the contrary, differ widely from each other. From this fact, it may be presumed, that in those cases in which these changes have been limited, death cannot be assigned to them, even if the urinary secretion should have been suspended for an abnormal length of time before this event took place. Even in those cases, in which these changes have progressed to a considerable extent, there is a sufficient number of uriniferous tubules left open for the passage of the secreted urine. And if, in some cases, a total suppression of urine really takes place, it is hardly due to the obstruction caused by the infarctions, but much more probably by the general *atrophy* and *degeneration* of the epithelium. But, even if this were the case, the question whether the suppression of urine is the immediate cause of death, as is believed by a large number of physicians, remains still undecided.

The question whether or not the nervous symptoms accompanying certain organic changes in the parenchyma of the kidneys, and called "uræmic," really depend upon an accumulation of

urea in the blood, has been agitated for a considerable number of years, and is as yet not definitely settled, though, in the course of this time several theories, in a modified form, have been advanced. Thus, while a number of physicians regard the accumulated urea in the blood as the immediate cause of uræmia, others accept the theory of *Frerichs*, according to which these nervous phenomena are owing to the carbonate of ammonia resulting from the decomposition of the urea in the blood; while others, again, attribute them to the presence of the extractive matters. *Traube*, even, rejected these theories altogether, and attributed the symptoms of uræmia, consisting in convulsions, coma, vertigo, etc., to œdema of the brain. Since these different theories were advanced, a considerable number of experiments and observations have been made in relation to the subject, for the purpose of ascertaining the truth, and almost all the results obtained rather prove the fallacy of the uræmic theory. I shall cite the views of some of these investigators. Thus, *Chalvet** found during the uræmic attack a diminution of the urea in the urine and blood, rising again after the attack, but without attaining the normal quantity. Accordingly, he rejected the theory of Wilson and Frerichs, based upon a retention of urea in the blood, and rather regarded the retention of excremental matters in general as the cause of the uræmic phenomena. He, moreover, doubted that urea was formed in the tissues at all, but were rather a secretory product of the kidneys. *Budde*,† who made quite extensive observations on this subject, opposes the uræmic theory based upon the poisoning by urea, and particularly points to the fact, that a diminution of the secretion of urea before and during the uræmic attack does not constantly occur. He says that it is true that such a diminution takes place with a simultaneous decrease of diuresis, though the latter is in many cases rather abundant during the uræmic state. Four cases, which the author himself closely observed and described, showed an abundant diuresis, and three of them, besides, an excretion of urea in a comparatively large quantity, namely: 25.7, 27.6 and 22 grms.

* *Virchow u Hirsch*—Jahresbericht f. d. Jahr, 1867, Vol. I, p. 336, and 1868, Vol. I. p. 226.

† L. c.—f. d. Jahr, 1874, Vol. I, p. 347.

In 25 severe and fatal cases of uræmia, which he collected, there were five with abundant diuresis up to the commencement of the attack, in one of which the diuresis even rose to from 1200–2000 Ccm. during the attack. The conclusion drawn from this is, that, even if the excretion of urea is considerably diminished, or temporarily ceases altogether, uræmia must not necessarily follow; it rarely occurs in amyloid degeneration of the kidneys, neither in a cachexia, as leucæmia, notwithstanding the very scanty excretion of urine in these cases. Finally, uræmia does not necessarily follow upon long persisting anuria, accompanying certain diseases of the kidney and urinary passages. Budde observed himself a case of anuria lasting 40 hours, not followed by uræmia;* he furthermore reports a case of a woman, of 24 years, with highly albuminous and abundant urine—during several ca. 1700 Ccm., a few times even to 2300 Ccm.—and considerable œdema, in whom slight uræmic symptoms were observed, disappearing again with the decrease of the œdema. Two weeks previous to death, severe diarrhœa and vomiting, accompanied by scanty urine and disappearance of the œdema, occurred; and in the last 132 hours total anuria with no discharge per os or per anum, and without any uræmic symptoms. The autopsy revealed: chronic nephritis in the second stage, amyloid degeneration of the spleen, bronchiectasis and phthisis cavernosus pulmonalis. The author then shows the untenability of the theory, according to which uræmia is caused by a poisoning through the extractive matters, or through the carbonate of ammonia, and endeavors to prove the incorrectness of the assertion of *Jaccoud*, that toxic uræmia clinically differs from that depending upon anæmia and œdema of the brain, and that the former can be recognized by an œdema otherwise wanting, as he found in his 25 cases of fatal uræmia six with œdema and anæmia of the brain without œdema in other localities, and six others with the same condition of the brain, and inconsiderable œdema in other places. For this reason, Budde sanctions the theory of *Traube*, which assigns

* A remarkable case of suppression of urine, observed by my friends, Drs. D. W. Brickell and J. D. Bruns, occurred very recently in this city. It was a boy, nine years old, who suffered from congestive bilious remittent fever, with a complete suppression of urine—duly ascertained by the use of the catheter—for 67 hours previous to death. His intelligence was perfect up to the instant of death, and no trace of uræmia was observed.

œdema and anæmia of the brain as the cause of uræmic phenomena. In order to show how frequent these changes in the brain are met with, he collected and tabled these 25 cases of fatal uræmia which he observed in the Communal Hospital of Copenhagen. In 18 of these cases, anæmia and œdema of the brain were found; in four others, accumulations of liquid in the ventricles and in the subarachnoid spaces of the brain were present; in two more there was anæmia alone, and in one only, the brain was normal. These statistics support the theory of Traube in a high degree.

More recent experiments, consisting in the injection of urea into the blood, have neither been followed by convulsions, but rather by a rapid excretion of the urea, proving what has been said before.

From the observations, cited above, together with others that occurred in this city, we have reason to judge that in those rare cases of yellow fever, in which a total suppression of urine really takes place, we are not justified in assigning it as the true cause of the convulsions, occasionally observed before death. A suppression of urine, therefore, can only signify an extensive degeneration of the secretory structure of the kidneys, the epithelium, and an exhausted condition of the nervous system, similar to the black vomit, indicating the desperate condition of the liver. At the same time, it must be remembered, that the secretory function of the kidneys is really not totally suppressed in all cases in which suppression is reported, but that, if they were properly examined, many of them would turn out to be only cases of retention, while in others the urinary function would be found to be only temporarily suspended. Thus it has frequently occurred that in cases in which the physician had even based his judgment upon the results obtained from the use of the catheter when pronouncing suppression, the secretion of urine had only been suspended, and was resumed soon afterward.* In many cases, however, suppression of urine is pronounced without the catheter ever having been resorted to. The fact that urine is

* *Dr. J. Dickson Bruns* reported to me a case, which he observed during the epidemic of 1873, and in which the secretion of urine was thus suspended for 36 hours, at the expiration of which time it was fully resumed.

found after death in the bladder in, at least, half the cases of autopsies, corroborates this assertion. We may then reasonably suppose, that though total suppression of the urine may take place in exceptional cases, it is not the immediate cause of convulsions and death, but that, on the contrary, the latter are owing to the diseased condition of the brain.

In the preceding section of this treatise I have shown, that in the numerous fatal cases of yellow fever in which I examined the brain, not only the smaller blood-vessels of the pia mater but also those of the brain ubstance itself, were found congested with blood, and that, in almost all of these cases, the congestion extended throughout the whole organ, and particularly throughout the pons varolii and medulla oblongata, in which the vaso-motor, trophic and secretory nerve-centers are situated. The hyperæmia of the brain depends upon the same cause as that of other organs, that is, upon a depression of the vaso-motor nerves, followed by a relaxation of the arterial walls. Gradually commencing before the beginning of the fever, it manifests itself already in the headache and general nervous depression during the preliminary or initial stage of the disease, but increases with the appearance of the fever, when the action of the heart becomes more violent, and when the arteries, in consequence of the relaxed condition of their walls, are no more able to withstand the increased pressure of the blood. And as these vessels cannot recover their normal tonicity as long as the battle between the organism and the infectious poison is raging, the congestion of the brain becomes persistent, and increases the already existing disturbance of the nutrition of the nervous tissues of this organ. In consequence, a considerable amount of the nervous energy, which in the normal condition is destined to supply the various organs, is now lost by being converted into heat, a condition which will last until the original cause of these abnormal processes, the noxious poison, is eliminated from the organism. If this condition of things lasts only a limited time, no organic changes will take place in the nervous tissues, but, on the contrary, they will, with the subsidence of the fever and the accompanying exchanges of matter, regain their integrity, as happens in all cases of recovery from yellow fever, and also in most other

cases of hyperæmia of the brain. In the more violent cases of yellow fever, however, in which the febrile process is prolonged and particularly stormy in character, the hyperæmia becomes persistent and manifests itself by violent delirium, convulsions, or other serious nervous phenomena, which have been regarded as depending upon the degenerated condition of the renal parenchyma, and the ensuing uræmia. That this is not the case, but that, according to the theory of Traube, they in reality depend upon an œdema, or any other diseased condition of the brain, deranging the normal functions of this organ, I have already sufficiently shown in the preceding pages, and can, moreover, corroborate by the œdema and anæmia of the brain which I observed, two years ago, in a man who had been for a number of years an habitual opium-eater, and who died under severe convulsions, to which he had already been subject before his death. In a number of fatal cases of yellow fever, the brain, as I have shown, is found œdematous, which here, however, depends upon a hyperæmia, a condition, it is true, opposite to that which Traube assigns to the uræmic convulsions. This apparent contradiction, however, is easily explained by the fact that some of the accompanying phenomena of anæmia of the brain, such as convulsions, may likewise be produced by a hyperæmia of that organ. In both cases, the symptoms depend upon a disturbance of the normal nutrition of the organ, arising, in the one, from a diminution, and in the other from a derangement, or complete interruption, of this function.

The deranged nutrition of the nervous tissues, caused by a persisting hyperæmia, will also eventually give rise to degenerative changes of these tissues, or their minute blood vessels. Such changes may be observed, in a number of fatal cases, in the fatty degeneration of the minute blood vessels and of ganglion-cells of the sympathetic ganglia, and, even, to some extent, in those of the cortex cerebri. The degenerations which I observed in the semi-lunar and first thoracic ganglia, consisting in the disappearance of the nuclei of the ganglion cells, and in the fatty and atrophied appearance which the latter themselves presented, cannot but exert a most deleterious influence upon the organs which they supply, by greatly diminishing the nervous energy

which they need for the preservation of their integrity. With the degeneration of the nuclei of the ganglion-cells, which I regard as special reservoirs, or stores, of potential energy, the influence which these nerve centers exert upon the nutrition of their respective organs, must become considerably diminished. The pathological changes in the kidneys, supra-renal bodies, and liver, therefore, may stand in a close relationship with those observed in the semi-lunar ganglion, and other ganglia of the solar plexus. In the same manner may the changes in the muscular tissue of the heart depend upon those in the ganglion stellatum. But, judging from these changes, found in those sympathetic ganglia to which my examinations extended, viz., the ganglion stellatum, ganglion semilunare, and some others of the solar plexus, we may well presume that they had equally taken place in a number of other sympathetic ganglia, especially those of the cardiac plexus; and if, furthermore considering that the nerve centers which regulate the action of the heart, as well as its nutrition, send their stimuli through the ganglion stellatum and cardiac plexus, it becomes obvious that these changes cannot but exert a depressive influence upon the action and nutrition of this organ.

Thus it happens that, while during the febrile stage of the disease the heart's action is accelerated by the irritative influence of the poison upon these centers and ganglia, it is depressed during the second, but particularly the third stage, when the nervous energy becomes abnormally diminished by these pathological changes and the ensuing exhaustion of the nerve centers. And if this nervous depression passes beyond certain limits, a collapse of the organism must evidently be the result; but it may also terminate in paralysis of the heart, causing the death of the patient. In very severe cases, the nervous depression is frequently associated with a degeneration of the muscular tissue of the heart, which is likewise cutting off every chance for recovery. Excessive nervous depression, or paresis of the heart is, therefore, one of the most dangerous symptoms in the whole course of the disease, especially when it appears in the last stage of the disease, as it may then be associated with the degeneration of the muscular element, and, if not soon relieved by stimulation,

must evidently lead to collapse. The feebleness and rapidity of the pulse, together with the diminution of the peripheral heat, especially of the extremities, indicate the approaching danger, the action of the organ being too low to properly circulate the blood through the peripheral vessels. The muddy, cyanosed appearance of the face, shortly before death, also depends upon this cause.

In taking a final review of the nervous phenomena of yellow fever, we find then that, while in the commencement of the disease they depend upon a paresis of the vaso-motor nerves, this condition is soon followed by an irritation of the different nerve centers mentioned, situated in the medulla oblongata, and giving rise to the temporary acceleration of the heart and the irregular contractions of the cutaneous blood vessels during the hot stage; but that, in the second and third stage, this abnormal excitation is relieved by a general depression and exhaustion of the nervous system, in many cases associated with paresis, or even paralysis of the heart. But though the latter condition, which mostly takes place in protracted cases, may be the immediate cause of death, the hyperæmia of the brain is not relieved, but persists in a more chronic form until the fatal issue, when its presence will be revealed by the autopsy. That in fatal cases, without regard to the immediate cause of death, the neuro-paralytic condition of the blood vessels persists until this event takes place, is corroborated by the larger cerebral arteries, even the basilar, being found filled with blood, which is not the case in other diseases in which death occurs from other causes and without hyperæmia of the brain, where the larger and smaller arteries contract during the agony, driving the blood through the capillaries into the veins.

The pathological changes, observed in the supra-renal bodies depend upon the same causes, and take place in the same manner as those in the kidney, liver, and other organs; but, for the reason that so little is known concerning the true function of these organs, I shall forbear making any remarks as to the part they may play in yellow fever.

In comparing the clinical phenomena and pathological changes of yellow fever with those of other infectious diseases, we find

that they resemble each other in many points. Thus, in the typhoid diseases, such as typhus, typhoid, bilious typhoid, and relapsing fever especially, the same nervous disturbances, caused by the influence of the infectious poison and the ensuing derangement in the nutrition of the nervous tissues, are equally met with. The extravasations of hæmoglobin and the general tendency to capillary hæmorrhage, as well as other degenerative processes in the glandular organs are also observed in numerous cases of these diseases. But, notwithstanding the similarity existing in the above phenomena, there are some other important points, in which yellow fever essentially differs from these typhoid or other kindred diseases. The difference particularly concerns the so-called "blood-making" organs, the spleen and the lymphatic glands, which in the above diseases are almost always more or less affected, while in yellow fever they remain perfectly normal. This circumstance also explains the fact, that in these infectious diseases the blood is frequently found to have lost its coagulability, that is, it has in the true sense of the word become contaminated, or prone to decomposition, which never, or, at least, *very rarely* takes place in yellow fever, though it is believed by a large number of physicians. In the latter, the infectious poison appears to exert its noxious influence especially upon the morphological constituents of the blood, the colored blood corpuscles, inducing them to part with their coloring matter, the agent in the processes of oxydation taking place in the organism; and the congestions occurring depend less upon a true contamination of the blood, than, as has been demonstrated, upon a paresis or paralysis of the vaso-motor nerves.

Another difference may be found in the duration of the febrile process, the extent of which seems to be typical, as regards its length of time, to each individual infectious disease.

Besides, many of the phenomena of yellow fever are also met with in those infectious diseases, known as "*exanthemata*," and in the different forms of miasmatic disease, so that only a few symptoms remain to be regarded as *pathognomonic* of this disease. This leads us to the question, How then, may yellow fever be distinguished from the above named diseases, and how may sporadic cases be correctly diagnosed during the absence of an

epidemic?—questions quite difficult to answer. In the commencement of the disease, and, even, after the febrile process has started into action, it is almost impossible to make an infallible diagnosis, as a number of other infectious diseases commence in the same manner, accompanied by the same phenomena. In the diagnosis of yellow fever, therefore, *the whole complex of symptoms must be taken into consideration.* On the second day, the general observation concerning the relative state of the pulse and temperature, to which I have referred before, may be applied. This observation consists, as will be remembered, *in the falling of the pulse on the second day*, *with a simultaneous rise of the temperature of the body.* The presence of albumen in the urine on the third day, also, may to a certain extent serve as a pathognomonic symptom. If the disease runs on to its third stage, and black vomit should appear, all doubts about the nature of the disease, of course, must vanish. In fatal cases, the autopsy must decide the question from the pathological changes met with in the different organs, for *fatty infiltration of the liver*, *associated with that peculiar congestion of the stomach*, *together with black vomit*, are pathognomonic phenomena of yellow fever.

As regards the prognosis of the disease, the reader may draw his own conclusions from what has been said in the preceding part of this treatise.

PART II.

REMARKS ON THE PROBABLE NATURE OF THE INFECTIOUS POISON OF YELLOW FEVER.

In the preceding part of this treatise, I first conducted the reader to the bed-side of the yellow fever patient, in order to take a general view of the clinical symptoms, such as they generally present themselves to the physician during an epidemic. After the study of these phenomena, I conducted him to the dead-house, and pathological laboratory, where I showed him the pathological changes in the organs and tissues which had taken place during the course of the disease; and lastly, attempted to draw a sketch of the complex of pathological processes constituting the disease, by comparing the clinical phenomena with the pathological facts revealed by the autopsy and microscopical examination, the whole representing the general pathology of yellow fever.

In discussing the latter, I frequently referred to the influence or effect of the infectious poison, the original cause of the disease, but forbore to make any remarks upon its particular nature, which I shall now discuss. While in the preceding pages, however, we dealt with substantial, incontestable facts, with phenomena or things of a tangible nature, directly appreciable to our special senses, we now approach a subject which, on the contrary, is, to a certain extent, hypothetical in its nature, and where, unfortunately, too much space is left for the vagaries of the imagination. With the exception of cholera, there exists no disease of which the original cause or contagion has given birth to such a variety of speculations, both among physicians and laymen, as yellow fever. Inorganic and organic nature, the earth, the water, the atmosphere, minute plants and animals, the planets, and even invisible germs, have been suspected to be the cause. And accordingly, especially during an epidemic, when the daily news-

papers are pregnant with yellow fever literature, there is no want of suggestions, and wise speculations, relating to that mysterious agent, the "germ" of the disease. In such times, high or low, wise or ignorant, everybody has an opinion, a view of his own on the subject, and without regard to whether it is based upon sense or nonsense. How cheaply feels the man of science and facts, the lover of truth and reason, in such a time. His voice is too weak to be heard in the turmoil, and all he can do is to observe and to collect, and to study the facts relating to the subject, to be conscientiously compared with those already established by other observers, at a time when the storm has passed, and the general excitement is worn out.

These remarks will not only show the difficulty, but, moreover, the delicate nature of the subject which I now propose to discuss; and if I fail in this task, it will not be owing to a lack of desire of presenting the subject fairly and without prejudice, but to my incapacity.

In the discussion of a subject, such as the probable nature of the infectious poison of yellow fever, of which the opinions of physicians differ so widely from each other, it is essential that the author should present it to the reader in all its various aspects, and be concise and definite in the terms of his demonstrations; while, on the part of the reader, in order to properly understand the arguments brought forward and to judge correctly, it is no less important that he should be familiar with the details of the subject. To comply with these propositions, it becomes necessary to introduce the subject with some general remarks.

As long as yellow fever has been known to the civilized world, a controversy has existed among medical men, especially among those of prominent seafaring nations, as to whether this disease is communicable from individual to individual, either in a direct or indirect manner, or whether its cause exists uniformly throughout the air of the infected district, having access to all persons alike. In other words, the question was, and still is—Whether yellow fever is a *contagious*, or a purely *infectious* disease.

As the terms "infection" and "contagion" have formerly been, and perhaps still are, by a number of physicians looked upon as synonymous, though they really convey different ideas,

some explanation is demanded in what sense they will be used in this treatise. As far as I understand their proper meaning, the term "infection" signifies that the disease has been acquired by some noxious body taken into the blood from *without*, and without regard to whether the infectious poison is a product of the animal organism itself, or, on the contrary, a body *totally foreign* to it, which, whether *animate* or *inanimate*, owes its existence to external causes, whatever they may be. The term "contagion," on the other hand, implies that the *active poison emanated* from the diseased person or animal, and, if entering the blood of a healthy individual, gives rise to all the symptoms and organic changes by which the original disease is characterized.

Now, it is obvious that a purely *infectious* poison, as, for example, that causing miasmatic fever, hardly ever exists limited to one particular spot or center, but is rather distributed throughout the whole air of the infected district, and affects many persons at the same time; while a *contagious* poison, like that of small-pox, being *most probably* a product of the diseased organism itself, originally emanated from the affected person or animal, and extends its noxious influence by being inhaled or swallowed by other individuals in the vicinity. From this common center the disease spreads, either *directly* from individual to individual, or *indirectly* by adhering to surrounding objects, such as clothes, bedding, furniture, goods, etc.; upon which it may be carried to distant places, and, as in the first instance, propagate itself by entering the system of other individuals.

From this explanation it will be seen that some poisons may, in entering the organism, give rise to certain diseases not communicable from individual to individual, and be therefore purely *infectious;* while others, producing communicable diseases, and being *contagious*, are at the same time *infectious*, as they must necessarily enter the blood of the individual before they can exert their noxious influence upon the organism, and manifest their contagious nature. But notwithstanding this general trait of character, possessed alike by the *purely infectious* and *contagious-infectious* poisons, the latter have a *special* trait besides, consisting in a certain permanency of the impression which they make upon the organism, and by which the latter acquires the so-called

"*immunity*" from a second attack of the disease. Accordingly, a *purely* infectious disease may recur quite frequently, while the first attack of a *contagious* infectious disease protects the organism from another.

Although many causes have in the course of time been assigned to the origin of the various infectious diseases, nothing definite is as yet known about the intimate nature of their infectious poisons. The most prominent theories, at present entertained on the subject, are—the "gaseous," the "glandular," and the theory of the so-called "contagium vivum." The first refers the poison to gaseous or molecular substances, arising from the decomposition of vegetable and animal matters, or even from certain emanations from the ground of certain localities, known as *miasmatic* or *malarial* poisons. The second theory explains the poison as being of an animal origin, similar to the poison of snakes or other animals, or produced by certain morbid changes in the blood and tissues, called forth by its original introduction, and giving rise to morbid secretions possessing its specific properties. The theory of the "contagium vivum," lastly, refers the poison to certain minute organisms, which, entering the system through the lungs, alimentary canal, or even wounds, get into the blood, and give rise to the specific symptoms of the disease. Each of these theories, of course, exists in different minor forms or variations.

Now, as regards the cause of yellow fever, each of these theories, with its minor variations, has been put forward for its explanation, but without any palpable or positive proofs; for if anything regarding it can be proved, it is only negatively. With a considerable number of physicians, the theory of the contagium vivum, or so-called "germ or bacteria theory," being of a more recent date, has become especially popular. But as its origin and details are, as it appears, least understood of all others, I shall give it the preference for a full discussion, from which the reader may judge for himself whether it is applicable to yellow fever or not.

The theory of a "contagium vivum," relating to the cause of infectious diseases, is not of a recent date, but seems to have existed as a vague idea since the invention of the compound microscope, by means of which the existence of minute organisms first became known to the physician. At the same time another idea

prevailed, according to which infectious diseases dependea upon a certain process taking place in the blood, similar to that of alcoholic fermentation. These ideas assumed a more definite form by the discovery of *Schwann*, that the yeast-cell played an active part in this fermentation. Nevertheless, the germ theory, thus formed, lingered for a number of years, until it received a fresh impulse by *Pasteur's* proclamation, that every fermentative process was called into action by the agency of minute organisms performing the part of a ferment, and that each kind of fermentation depended upon a special kind of fungus. Pasteur's views, of course, were in opposition to the physico-chemical theory of *Liebig* then prevailing, according to which any organic matter. while in a state of decomposition, was able to induce molecular changes in another unstable, fermentable substance. Now, although the assertions of Pasteur, that all fermentations are accompanied by living organisms, have been generally admitted as a fact, the question, whether these organisms are the direct cause of the molecular changes, or whether they are to be regarded as epiphenomena, remains as yet undecided, and the theory of Liebig is, in a slightly modified form still upheld by a number of the most eminent chemists.

The doctrines of Pasteur were eagerly received by many physicians, and applied to the explanation of the cause of infectious and contagious diseases. The greatest impulse, however, which the germ theory received, was the discovery and description of minute organisms in the blood of animals affected with malignant pustule or splenic fever, by *Pollender* and *Brauell*, in Germany, a subject which, several years later, was more closely studied by *Davaine* in France.

A still more definite form the germ theory received by the examinations of cholera-stools, made by *Klob* during the epidemic prevailing in Europe in the years 1865 and 1866. In examining, namely, the intestinal contents of cholera patients, he discovered a large number of very minute spherical bodies, together with others of a more oblong form, adhering to the outer surface of the epithelial cells. In the intestinal mucus, or in that of the cholera ejections, he also met with these bodies, collected in circumscribed patches in the form of so-called colonies, and imbed-

ded into a gelatinous material. In certain parts of these colonies he observed a number of these bodies, liberated by the liquefaction of their gelatinous envelope, in active motion; while others, united in pairs, or adhering to each other in the form of longer or shorter rows, remained motionless. In the intestinal mucus he met with such colonies formed by oblong, rod-like bodies, either in pairs or, like the former, united into chains of different length.

From these observations, Klob drew the conclusion that all these bodies represented but a single organism in its different phases of metamorphosis, and by further inquiry found them, especially the rod-like form, to correspond with the *Zoglœa termo* of *Cohn*, or *Bacterium termo* of *Dujardin*. Meeting, however, with no other vegetable organism in the ejections, but always with large numbers of these bacteria, he concluded that these forms of fungi, constantly met with in the alimentary canal of cholera patients, never attained a higher development in this locality.

From this it will be seen that these bodies represented the same organisms always met with in stale urine, and other putrid substances, formerly known to physicians under the name of "vibrios," though the knowledge of their true nature and development, and the prominent part which they play in the process of fermentation, belongs to more recent times. They were already known to *Ehrenberg*, who regarded them as animals, and classed them with the *Infusoria;* but when their nature was rendered doubtful, *Haeckel* placed them, about thirteen years ago, in his newly established natural kingdom of *Protista*, composed of a number of other organisms of doubtful origin. *Naegeli*, a distinguished German botanist, formed them into a separate group of fungi, which he named *Schizomycetes*. In classing these organisms with the lower forms of fungi, however, a difficulty was encountered in the want of similarity regarding the precise mode of their reproduction, for while, with the exception of *Cryptococcus cerevisiœ*, or yeast plant, in all fungi certain typical organs of reproduction are known to exist, none could be demonstrated to exist in the schizomycetes. For, in the latter, the only mode of multiplication observed, consisted in a division of the minute rods in only one direction, while in the fungi, which are likewise rep-

resented by linearly arranged cells, the process of multiplication takes place by gemmation, not only in a straight line, but also by the formation of lateral branches. Finally, after having been studied and classified by other distinguished botanists, a second mode of reproduction, to be mentioned hereafter, was discovered in these organisms only a few years ago by artificial cultivation. In accordance with the importance they gained, their nature and their relations to organic substances were studied more closely, leading to the discovery of a large number of new species, and rendering the field they occupy so extended as to form at present a special branch of study in natural history. They have also been subjected to new classifications, especially by *Billroth* and *Cohn*, too extensive to be followed by the practicing physician. But, as in a few instances, particular forms of bacteria are found associated with some special pathological processes occurring within the animal body, and also with the different kinds of fermentation observed in fermentable substances, I deem it proper to give a short sketch of the lower fungi in general, and of those species of the schizomycetes in particular, which have hitherto been observed in association with these processes.

As regards the lower forms of fungi in general, *Prof. Naegeli*,* of Munich, one of the first authorities in Botany, divides them in three natural groups, as follows:

1. *Moulds*, representing branched, segmented or unsegmented filaments.

2. *Sprouting fungi* (yeast-cells, saccharomyces, mycoderma, etc.), representing spherical or oval cells, multiplying by means of sprouts from their surfaces, and living either singly or united to form arborescent colonies.

3. *Cleft fungi* (schizomycetes, putrid-fermentation cells, micrococcus, bacterium, vibrio, spirillum, etc.), are spherical cells multiplying by division, and met with either singly or united into rows (rods, filaments), rarely into cubes. They represent the smallest organisms known, the weight of 30,000 millions of the smaller forms would scarcely amount to one milligram.

" The moulds slowly destroy organic substances by consuming

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*C. v. Naegeli. *Die niederen Pilze in ihren Beziehungen zu den Infections Krankheiten und der Gesundheitspflege.* Muenchen, 1877.

them for their nutrition, while the sprouting and cleft fungi act besides as ferment in decomposing large quantities of matter by fermentation."

"The moulds and sprouting fungi are closely related, though, with the exception of one case in which the same fungus (mucor) appears in two forms of vegetation, they have as yet not been directly traced from one form to another. The cleft fungi, however, stand in no genetic relationship to the two other groups, as they can neither produce other forms of fungi, nor take their origin from these."

"The natural species of the lower fungi are not developed in such a manner as to have particular functions of decomposition corresponding with them. If there are different species existing among the cleft fungi, then each of them will cause different decompositions, as, on the other hand, the same decomposition may be caused by different species."

The following classification of the *Cleft fungi* or *Schizomycetes*, will suffice for all practical purposes.

The most simple form in which bacteria are met with is that of minute spherical or oval granules or cells, designated by *Cohn* the *sphæro-bacteria*. These are identical with the *micrococci* of *Hallier*, measuring from $\frac{1}{1000}$ to $\frac{1}{1200}$ mm. in diameter, and are often found aggregated into so-called "zogloea" or colonies, held together by a gelatinous intercellular substance, or, also, forming bead-like chains. They are motionless, and are sometimes found in putrefying substances in company with other bacteria, and and have also been considered identical with those granules found in the vaccine lymph.

The next group is represented by *bacterium termo* and *b. lineola*. The first presents the form of a minute rod or dumb-bell, has a slow, vacillating motion, and measures from $\frac{1}{360}$ to $\frac{1}{480}$ mm. in length; it is always found associated with putrefactive fermentation. The other is somewhat larger, and exhibits more rapid movements, being found, in company with b. termo and other forms, in stagnant water, as also in putrefying infusions.

The members of the third group are distinguished from the true bacteria by adhering to each other in the form of chains or "linked rods." It consists of *Bacillus*, representing a trans-

versely lined filament, and of *Vibrio*, appearing as a cylindrical and curved filament. There are three species of *bacillus*. The first is *b. subtilis*, a slender thread, about $\frac{1}{20}$ mm. in length, and exhibiting a pausing motion. The second, *b. anthracis*, or *bacterium carbuncolare*, represents a motionless, oblong, and highly refractive body, found in the blood of animals affected with splenic fever, and measures from $\frac{1}{400}$ to $\frac{1}{80}$ mm. in length. The third is *b. ulna*, a stiff filament of $\frac{1}{26}$ mm. in length, and of greater thickness than *b. subtilis*. The *vibrios* are distinguished from the preceding forms by their rotary motion. The *v. regula* represents a flexible thread, from $\frac{1}{100}$ to $\frac{1}{43}$ mm. in length, distinguished by one or two slight curves and its slow motions. The other, *v. serpens*, measuring about $\frac{1}{80}$ mm. in length, is thinner than the preceding, and distinguished by the greater number and regularity of its curves and its more rapid serpentine motion.

The fourth group consists of the *spiro-bacteria*, distinguished from the vibrios by the greater regularity and closeness of the curves of the spiral, and their uniform, cork-screw motion. They are represented by *spirochaete*, to which the spirilla, found in the blood of relapsing fever patients, belong; and by *spirillum*, fine threads of a cork-screw form with a rapid spiral motion.

Nearly at the same time with Klob, *E. Hallier*, a professor of Botany in Jena, had also made a number of microscopical examinations of cholera stools, and for some time agitated the medical world by the discoveries he claimed to have made, consisting in certain spherical and oblong vesicles, filled with minute yellowish and glistening cells or spores, and also of certain spherical masses of minute roundish bodies, held together by a homogeneous gelatinous substance. To the granules or cells of these masses (colonies), adhering in large numbers to the remains of food and to epithelial cells, Hallier applied the name of "Micrococcus." Obtaining almost the same results from other examinations of cholera stools and vomited matters, sent to him from other places, he undertook, by certain methods, to cultivate the fungous elements they contained; and after the lapse of several days, he really found an increase in the forms of micrococcus, cryptococcus, torula, and leptothrix. In some of these cultures only certain forms of fungi appeared, while in others, other forms were ob-

served, such as oïdium lactis, mucor racemosus, and also penicillium glaucum.

These examinations, made upon old material, could not have, as will be readily understood, any important bearing upon our knowledge of the cause of cholera, and for this reason could not but meet with much opposition and criticism on the part of other investigators. Nevertheless, Hallier drew from these observations the conclusion that those minute granules of micrococcus were able to give rise to various forms of fungi, and, moreover, that the particular form of a fungus depended upon the particular material in which it was cultivated. Thus, from each species of fungus micrococcus spores might be derived, which, according to the nourishment they received, would be developed into one or the other species of fungus.

Thus far, the whole question concerning the metamorphosis of one species of fungus into another would have remained botanical in its nature, if Hallier had not extended the bearing of his observations to the field of medical science in asserting that all infectious diseases were caused by the presence of micrococcus spores penetrating into the capillaries of the human organism, in which they multiplied, without ever being developed into a perfect form of fungus. Accordingly, each form of micrococcus would give rise to a particular disease. The same theory he applied to the process of fermentation, in which, according to the nature of the fermentable substance, a different fungus was produced. The application of Hallier's fungi theory to the causes of infectious diseases met with considerable opposition in Germany; and being finally rejected, made room for the so-called "bacteria-theory," which, though *apparently* supported by a few observed facts, to be discussed directly, is still very far from being established as a truth applicable to all infectious diseases.

Let us now take a glance at those diseases in which bacteria are almost constantly met with in the blood of the affected individuals. There are, in reality, only two in number—viz., splenic fever, and typhus recurrens, or relapsing fever,—to which may be added purulent septicæmia, and pneumo-enteritis of the pig, described by *Klein*. In the latter, however, *no bacteria are found in the blood of the diseased animals;* they can only be ob-

tained from the inflammatory exudations by artificial cultivation. Besides, bacteria have *occasionally* been found in the blood of diphtheritic patients, and also in the vesicles of vaccina and variola. The first and last of these diseases are confined to our domestic animals, though splenic fever is also communicable to man.

In examining these diseases separately, we shall begin with *splenic fever* (malignant pustule, anthrax), the disease in which bacteria were first discovered in the blood of the affected individuals. It is chiefly met with in the sheep, cattle, hogs and horses, but may also be communicated by inoculation to smaller animals, as the rabbit, guinea-pig, mouse, etc., and even to man. It has frequently appeared in the form of an epidemic, spreading over certain districts, but is mostly confined to certain rural *localities*, even particular *pastures* or *stables*. The animals affected with the disease usually die one, two, or three days after the appearance of the first symptoms. One particular form of the disease, called the "apoplectic," is, however, observed, which proves fatal a few hours after its appearance. Death is accompanied by dyspnœa and cyanosis; and the chief anatomical changes revealed by the autopsy are enlargement of the spleen, a laky, viscid, dark-colored blood, numerous ecchymoses in different organs, especially in the heart, hæmorrhagic infiltrations into the areolar tissues, and also hæmorrhages into the alimentary canal. The particular phenomenon, however, now looked upon as pathognomonic of the disease, and bearing directly upon our subject, are the *bacteria* (bacillus anthracis) almost invariably found in the blood of the affected animals, in which they were first discovered and described by *Pollender*, more than twenty-five years ago, and the discovery corroborated soon after by *Brauell*. But it was not until several years afterward that the subject was taken up, and more closely investigated by *Davaine*, *Colin*, *Pasteur*, and, of late years, by very numerous other observers.

The statements of Davaine, that these bacteria represented the primary cause of splenic fever, and which first attracted the general attention to this subject, met for some years, however, with considerable opposition. Thus, when in 1869 the French Government appointed a commission, consisting of *Bouley*, *Teilhard*,

Lethérisse, *Maret*, *Tournadre*, *Bonnet*, *Baillot*, *Chauveau*, *Richard*, *Felgéres*, *Messonier* and *Sansom*, to investigate the cause of this disease, Bouley, the chairman, reported as follows: 1. That the disease will be produced by inoculation, even with blood containing no bacteria; 2. That the anthrax blood, containing bacteria, loses its violent properties by dessication, without regaining them by the addition of water, though the bacteria may still be present; 3. The blood of rabbits dying from splenic fever always contained bacteria, whether the disease had been produced by inoculation with blood containing bacteria, or with blood containing some of these organisms. Finally, experiments made by inoculating calves and sheep, showed that bacteria were not always present in the blood, and that the blood proved equally virulent, whether containing bacteria or not.

Now although in the majority of cases of splenic fever bacteria are met with in the blood and tissues of the animals, there have been, nevertheless, a number of cases observed in which they could not be found, and others in which they could only be discovered shortly before or after death, a circumstance which gave rise to many doubts as to whether these organisms were really the primary cause of the disease, or whether they were to be regarded as epiphenomena. These exceptional cases, however, were explained, only a few years ago, by *Koch*, who, by artificially cultivating the bacteria in the anthrax-blood, discovered that the rod-like, motionless bacterium lengthened into a filament, in which finally a number of very minute bright spores appear. These, when liberated by a disintegration of the filament, develop into other rods, and when introduced into the blood of an animal, rapidly increase by transverse fission. From these observations it was supposed that in those fatal cases of splenic fever in which, in the beginning of the disease, no bacteria had been met with, the germs only had been present, to develop into rods shortly before death.

Notwithstanding this discovery, the question was still disputed, and gave rise to the most animated discussions in the medical-scientific world, and to very numerous investigations upon the subject, with hundreds of experiments upon various kinds of animals. Thus facts were brought forward from one side, to be dis-

proved and contradicted from the other. But in carefully studying the results of the numerous investigations, the impartial observer must confess that in splenic fever, at least, it *appears* that the noxious influence upon the organism must be attributed to the presence of these bacteria. Perhaps the strongest proof of this assertion was forwarded, several years ago, by Davaine, consisting in the fact, afterward corroborated by others, that in pregnant animals the blood of the mother, containing bacteria, will, if introduced into the blood of a second but healthy animal, give rise to the same disease, and moreover cause certain death; while the blood of the fœtus is free from bacteria, and unable to reproduce the disease in another animal or to cause death. The placenta, therefore, performs in this case the part of a natural filter, allowing the liquor sanguinis to pass through it and enter the circulation of the fœtus, while the bacteria with the blood corpuscles are kept behind in the blood vessels of the mother.

Strong as this fact appears to be in favor of the correctness of the bacteria theory relating to splenic fever, it has not been sufficient to dispel all doubts on the question, which will probably not be satisfactorily solved until the origin of these particular bacteria is positively known,—that is, until it has been decided whether the affected animals receive them from the air they breathe, or from the water they drink, or whether they are contained in the ground of the infected pasture; and, lastly, whether they may not spontaneously be formed from organic granules, set free by the disintegration of some of the tissues within the animal itself, representing the process of "heterogenesis," as proposed by *Bastian.*

As regards their presence in the air, I have not met with any statement relating to it in the literature of splenic fever within my reach; though, regarding this matter, *Bender* suggested, a number of years ago, that these organisms might be contained in the green slime frequently covering not only the wooden troughs, but also the buckets and other wooden vessels containing the drinking-water of animals. *Bollinger*, who closely studied the epizoötic of splenic fever, prevailing some years ago among the domestic animals of the Bavarian Alps, states that in the Alps, as in all other places where splenic fever prevails, the condition

of the ground plays a prominent part, inasmuch as the swampy and moist terrain of the Alpine pastures, like that of the valleys, favors the conservation and reproduction of the infectious poison, and that splenic fever never arises primarily from the ground, but is only produced when the latter has been previously impregnated with the poison, and that the so-called miasmatic origin of splenic fever cannot be proved. He thinks that the dung of the diseased animals plays a more important part than is generally imagined.

Davaine made some experiments for the purpose of showing that the splenic fever poison was transmitted from one animal to the other, and even to man, by the proboscis of flies; his statements, however, have been contradicted as well as confirmed by other observers.

Acknowledging the probability that in splenic fever the bacteria, themselves, represent the infectious poison, I forbear citing the numerous experiments, made by Pasteur and others, for the purpose of deciding the question, and the interesting discussions to which they gave rise, but dismiss the subject by reminding the reader of the fact, that these bacteria differ in some respects from those which have been met with in the other diseases mentioned; though *Ewart*,* one of the later investigators of the bacillus anthracis, states that micrococcus-forms, bacterium-forms, bacillus-forms, and spore-bearing hyphæ are in nowise generally distinct, but that they are simply phases of the same life-history,—a life history doubtless common to all other bacteria.

The next disease to be considered is the *Typhus recurrens*, or so-called "relapsing fever," a contagious and epidemic disease, principally occurring in Germany, Russia and Ireland, but also in India; it is accompanied by affections of the spleen, liver, intestinal glands and kidneys, and by hæmorrhages in different organs. In the fever the pyrexia, lasting from two to six days, is followed by an apyrexia of eight or nine days; then follows a second paroxysm or relapse, lasting four or five days, and terminating in a profuse perspiration. Some cases terminate after the second paroxysm, though in many others other paroxysms are observed to occur. But the characteristic phenomenon of this

* Quarterly Journal of Microscop. Science, April, 1878, p. 168.

disease consists in the appearance of minute filamentary organisms in the blood of the patient, first discovered several years ago by *Dr. O. Obermaier*, of Berlin. These organisms, called *spirochaete*, or *spirilla*, represent exceedingly fine and delicate filaments, from $\frac{1}{100}$ to $\frac{5}{100}$ mm. or more in length, appearing and moving very rapidly in the form of a close spiral, similar to a cork-screw. They are only observed in the blood shortly before and during the period of pyrexia, while during the apyrexia or intermission, they are entirely absent; neither can they be discovered in any of the secretions of the body. The singular relation existing between the appearance of these spirilla in the blood and the paroxysm of the fever, naturally suggests the idea that they probably are the true cause of the latter; and the explanation of the appearance and disappearance of these organisms in the blood of relapsing fever patients is, that while the spirilla die at the end of each paroxysm of fever, they leave their spores behind, from which during the apyrexial period, a new brood arises; these spores, however, have *as yet not been discovered.* As regards the transmission of the disease from one individual to the other by inoculation with the blood, the statements are contradictory, though it appears that it can be done, provided the blood is taken from the patient during the period of pyrexia. At the same time, however, the same results were obtained by inoculation with blood containing *no* spirilla, and taken from cases not differing from the others in severity.

In the July number, 1879, of the *Quarterly Journal of Microscopical Science*, an article, entitled, "The *Microphytes* which have been found in the *Blood*, and their *Relation* to *Disease*," by *Timothy Richards Lewis*, M.D., Surgeon, Army Medical Department, Fellow of the Calcutta University, was published, which originally formed part of the Memoir on the Microzoa and Microphytes of the Blood, appearing as an Appendix to the "Fourteenth Annual Report of the Sanitary Commissioners with the Government of India." This paper, in which Dr. Lewis, who is sufficiently known as an authority on this subject, discusses the whole germ-theory in an able manner, has attracted considerable attention; and since, as regards "relapsing fever," he speaks from personal experience and observation, I shall take the liberty of

citing some of his remarks. He puts the question, why we should not at once admit that splenic disease is caused by bacteria rods, and that the aim of treatment should be the destruction of the vitality of these rods; or that recurrent fever is caused by screw-bacteria, and such remedial measures resorted to as tend to destroy them. Answering this question, he says:

"Before such views can serve as the basis of anything like rational treatment, it must be shown—1, either that these organisms, as ordinarily met with, are injurious when introduced into the animal economy; or, 2, that the forms found in disease are in some respects morphologically different from those known to be innocuous—such a difference, at least, as Virchow suggests, as exists between hemlock and parsley."

"With regard to the first point, it has been shown over and over again that all the representatives of the group of fission-fungi can be introduced into the system with the greatest impunity. Not only is their complete innocuousness practically put to the test by every individual at every meal, but observations have been published which have conclusively demonstrated that they may be introduced directly into the blood by injection into the veins, or indirectly, through the lymphatics in the subcutaneous tissue, without the slightest evil consequences. These facts are so well known and generally accepted that it is not necessary to refer to special observation."

"With regard to the second question, however, diametrically opposite opinions are held—all the advocates of the germ theory with very few exceptions, maintaining that the particular organism, in the particular disease in which they are specially interested, is wholly distinct from all others; that is, if the organism happens to be anything more definite than a granule or molecule. The diseases which have been specially cited as being associated with microphytes may be divided, roughly, into two classes, according to the form of the attendant microphyte — the septinous group, consisting of malignant pustule, septicæmia, and the malignant erysipelas or "typhoid" of the pig, on the one hand, and a low form of fever, commonly known as typhus recurrent, bilious remittent, etc., on the other."

"With reference to the organisms which have been found asso-

eiated with tho first-named group, taking malignant pustule as the type, it is to be observed that Mr. Robin in 1865 pronounced the bacteridia of Davaine to be identical with Leptothrix buccalis; and the well-known botanist Hoffman has stated his opinion that they do not differ from like bodies which appear in milk and in meat solutions. Ferdinand Cohn, again, in his observations as to the growth of bodies of the same character in hay solutions, declares that the bacilli in the latter are identical in form and size with those found in splenie disease, and that the various stages in their development correspond in every particular — the only difference which distinguishes them being that, whereas bacillus anthracis presented no movements, the bacillus of hay solutions did. This distinction, as has already been stated, has disappeared."

"Several years ago Dr. Cunningham and myself were, whilst conducting various observations together, frequently struck with the rapidity with which organisms appeared in the blood and tissues of animals after death in this country. The microphytes were not limited to minute spherical and elongated bacteria, but there were also present well marked staves and filaments. In a report submitted by us in 1872, and again in 1874, we drew attention to this matter and suggested the similarity between them and Davaine's bacteridia."

"A short time ago a circumstance occurred which drew my attention in a special manner to these organisms. Mr. Hart, a veterinary surgeon in Caleutta, forwarded to me for examination a little perfectly fresh blood which he had removed from a horse whieh had died that day of well marked anthracoid disease. His curiosity had been aroused as to the microscopical characters of the blood by perusing an account, in the *Veterinary Journal*, of 'worms' having been found in the blood of horses suffering from a similar affection in the Punjab. A slide was prepared and examined under the microscope at once, but no marked peculiarity could be detected; but when this and other slides were re-examined twelve hours later, having in the meantime been kept under a bell-glass, numerous staves and filaments were observed, which, as to size and form, accurately corresponded with the description

of like bodies characterizing the blood in anthracoid disease of Europe."

"Several cultivations were started by adding a little of the blood to fresh aqueous humor. The preparations were then set aside for a few hours in a moist chamber. As the temperature of the atmosphere at that time was generally over 90° F., no special appliances were necessary for supplying artificial heat. The development of the rods into filaments and subsequent appearance of highly refracting oval bodies in the latter, corresponded so completely with what Cohn, Koch, Ewart and others had described, that it is not necessary to give figures of the changes that took place. A series of such cultivations was conducted by transferring a little of the last cultivation to fresh aqueous humor, and so on from one preparation to the other."

"It was then determined to ascertain whether the bacilli found in the blood of animals, which had been set aside for a few hours after death, would manifest, under like conditions, similar changes during their growth. Rats were obtained, killed by means of chloroform, and set aside for from three to twenty-four hours, or longer, according as the temperature of the atmosphere was high or low. The results proved that, almost invariably, bacilli were to be found in their blood, in the spleen and in other organs. On one occasion the rapid appearance of organisms after death was exemplified in a somewhat remarkable manner, and possibly the mode of death was not without some influence in determining their exceptionally early and plentiful appearance."

"The man employed to procure the rats, determined that he would get a sufficient number to last for some time, and proceeded to a large granary with his rat-traps. Having, however, found that he could procure more than could be accommodated in the cage which he had brought with him, he obtained a large earthen vessel, transferred twenty-seven rats into it, and tied a piece of cloth over the mouth of the vessel. As may be supposed, the rats had perished before he got home—all except one."

"I examined the blood and the spleen of twenty of these rats, within about six or eight hours after their having been caught, and found in each case that there were innumerable bacilli present, in every way morphologically identical with bacillus anthra-

cis. In some of the cases the number was astonishing. They were present chiefly in the form of rods, but here and there some were seen to have grown to such a length as to cover two fields of the microscope."

"This experience tends to give support to the statement made by M. Signol before the French Academy, to the effect that motionless bacilli, identical with those found in carbon, will be found in sixteen hours or less after death in the blood of animals which have been asphyxiated by means of a charcoal fire. M. Signol, moreover, found that eighty drops of this blood would kill a sheep or goat very rapidly, notwithstanding that putridity could not be detected, so far as appearance and odor went; but that bacilli would not be found in the blood of the inoculated animals, either before or immediately after death."

"It has been urged that the microphytes which appear in the blood after death simply make their way into it from the intestinal canal as a result of the breaking down of the tissues. This objection is certainly no longer tenable, for many observers have shown that if some of the organs be removed from the body immediately after death, or indeed isolated from the circulation whilst the animal is still alive and under the influence of chloroform, these organisms will nevertheless appear if the preparation be kept for some hours at a suitable temperature."

In discussing the probabilities in favor of the bacilli and spirilla of the blood being epiphenomena, Dr. Lewis remarks:

"There is one circumstance in connection with the microscopic appearance which these organisms sometimes present, which deserves special mention, as it may serve as an explanation for their sudden disappearance from the blood; and that is, that they may present a well marked beaded or rosary-chain appearance. This feature I was able to observe on one occasion only. The spirilla of the ordinary character were plentiful in this person's blood on the evening previous to the day on which this observation was made, but when examined on the following morning, there were only linked or rosary-chain spirilla in his blood. They were not very numerous, and their movements were not of that *rushing* character ordinarily observed, but conveyed the impression of tumbling across the field."

"The inference which such an observation appears to warrant is, that when the blood acquires a certain as yet undetermined condition, it becomes unadapted to the existence of spirilla, and that the fibrils thereupon undergo segmentation, after the manner of other schizomycetes, and the separate plastides become diffused throughout the circulation; possibly, they then gradually disappear in the same manner as we have seen other plastides (minute bacteria, etc.) disappear after being injected into the circulation. This appears to me the more probable than that they continue in the circulation until the blood re-acquires the state suitable to their growth into fibrils, seeing that the time for their return is so uncertain—it may be two days, may be six days, or a fortnight even, and perhaps they may not return at all. Be that as it may, it is clearly evident that their existence as spirilla is dependent on the composition of the fluids of the body."

"Heydenreich suggests that their disappearance is due to the elevated temperature of the blood at the height of the paroxysm. If that were the case, they ought to become more numerous with the fall of the temperature after death, but it is well known that they disappear exceedingly rapidly when life becomes extinct, in this respect offering a marked contrast to other members of the cleft-fungi group—bacteria and bacilli."

"The fact of their total disappearance immediately after death, probably even before death actually taking place, is very significant, as showing the extremely close relation which exists between them and the blood in *living* tissues, seeing that when the blood is removed from the body, the spirilla will, under favorable conditions, retain their power of locomotion for several hours or days. What these subtle changes of the blood during fever processes may be, chemistry and physiology have not yet revealed; we can therefore only judge of them by the changes of temperature, etc., of the patient; and, in the particular condition under consideration, by the occasional appearance and re-appearance of spirilla, whose presence is manifestly dependent on antecedent changes. That the temperature commences to rise, and that other subjective symptoms are manifested before the appearance of spirilla, testifies to this, for it cannot be that they can exert an influence before they are themselves existent."

"Dr. Charles Murchinson, at the discussion on the germ-theory of disease at the Pathological Society, put this matter very closely when he said: 'The fact that in relapsing fever and sheep-pox distinct forms of bacteria have been found, in no way proves any casual relationship between these diseases and the bacteria, and is readily accounted for by the acknowledged fact that the form taken by many minute growths depends not upon the germ, but upon the nature of the medium in which it grows. Indeed, the observations which have been made on the spirilla of relapsing fever are strongly in favor of this view, for they are present in the blood during the first paroxysm, but disappear before the crisis; are absent during the intermission, but return with the relapse of the fever, and again disappear before the crisis. It seems difficult to account for their appearance and annihilation twice over, except on the supposition that the soil was suitable for their development during the febrile process, and unsuitable when the febrile process was complete.' A like conclusion must be arrived at regarding the bacilli in malignant pustule, septicæmia, and the so-called typhoid fever in the pig, horse and other animals. With regard to the microphytes just named, it may be confidently stated that they are never to be detected in the earlier stages of the disease, but only at a brief period before and after a fatal termination. To my knowledge they have never been found in the blood of animals which have subsequently recovered; they have always been recognized only as one of the concomitants of impending dissolution."

The next disease in which bacteria have been met with in the blood is *Septicæmia*, representing a depraved condition of the system, and generally observed in connection with grave surgical injuries, such as extensive wounds, etc., or following some operations, a condition characterized by all the symptoms of blood-poisoning. The anatomical changes observed after death are as follows: Early decomposition, skin of a dirty yellowish tint, with numerous livid spots, due to local congestion. Blood of a dark color, fluid, or imperfectly coagulated; small extravasations found in the heart. The lining membrane of the heart and aorta is more or less stained by imbibition of the coloring matter of the blood. The spleen is usually large and soft, very friable and

pulpy; the parenchyma of the liver and kidneys is congested or undergoing more or less granular degeneration. In a number of cases, metastatic abscesses are found, especially in the lungs and liver. In surgery, septicæmia is identical with pyæmia, a condition which for a long time was supposed to depend upon the absorption of pus from the surface of the wound into the blood. Though it remains doubtful whether healthy pus could produce this condition, it appears to be generally accepted that the infectious poison enters by the way of the wound, to give rise to a putrid infection of the whole organism, accompanied with or without the formation of metastatic abscesses. But, as in the latter, which are supposed to be formed by embolism, bacteria were found in many cases, this fact was taken hold of by the germ-theorists, and the question arose, whether the septicæmic phenomena were due to the absorption into the blood of a specific septic poison, arising from putrid changes in the pus secreted from the granulating surface of the wound, or even to a putrid decomposition of certain emboli in the blood vessels; or to the noxious influence of *bacteria* contained in the surrounding air and finding their way into the blood through the surface of the wound. The antiseptic dressing of *Lister* is based upon the assumption that the bacteria, settling upon the wound, cause a putrefactive fermentation in its secretion, which, if absorbed into the blood, gives rise to the symptoms characterizing septicæmia.

The idea that septicæmia depended upon the presence of a putrid poison in the blood gave rise to very numerous experiments made upon animals for the purpose of artificially producing this condition by the inoculation or injection of various putrid substances, such as putrefying blood, muscle, urine, etc., containing numerous bacteria, and, as was expected, resulted in the production of the same or similar symptoms and pathological changes in these animals, as characterize septicæmia. While some of these animals died, others remained unaffected. When, however, the blood of these animals, *containing bacteria*, was inoculated into others, graver symptoms, terminating in death, were produced, showing that the putrid poison had increased in violence, but without *being accompanied by bacteria.* Davaine, who extended this successive inoculation upon a very large number of animals,

found that the intensity of the poison was increased with each animal through which it passed, and that thus the one trillionth part of a drop would suffice to kill a rabbit. The latter presumption, however, has been refuted by Chassaignac, Onimus, and others. The pathological changes found in animals killed with septicæmic blood are similar to those of septicæmia in man. They are: peritonitis, pleuritis, enlargement of the spleen, pneumonia, hyperæmia of the kidneys, jaundice, and hyperæmia of the intestines. But while bacteria are almost always found shortly before or after death in the blood of animals inoculated with anthracoid blood, it is only an exception to the rule when they are met with in the blood of animals inoculated with septicæmic blood. In fact, all symptoms of septicæmia may be observed, *without the appearance of bacteria in the blood.* The bacteria found in septicæmic blood or abscesses mostly belong to the first group, the sphero-bacteria, and are generally met with in the form of zoglœa-patches. In fact, with the exception of splenic and relapsing fever, it is almost exclusively the micrococcus form that has been met with in other diseases, wherever bacteria have been met with in the blood and secretions, or upon suppurating surfaces. And it is especially this fact which the germ-theorists have hitherto failed to bring into harmony with their theory.

As in splenic and typhus recurrent fever, in septicæmia, also, the question has been whether these bacteria, found in a number of cases, are the direct cause of the disease, or mere accidentally accompanying phenomena; or, whether the symptoms of the disease depend upon the influence of a noxious poison formed within the organism itself. In order to decide this question, various experiments have been made, too numerous to be cited in this place. In these experiments, the most difficult part was to effect a separation of the bacteria from the putrid liquid containing them, and different methods have been followed to accomplish this task, one of which, first resorted to by Pasteur, consisted in filtering the liquid through porous substances, like burnt-clay vessels, by which proceeding the bacteria were left behind in the residue upon the filter. Separate inoculations with the filtered liquid or with the residue, were then made upon different animals, but as the statements of the results of these experiments are so

contradictory, I forbear mentioning them; for while, on the one hand (Pasteur) it is stated that the filtered liquid had lost its virulence, we are told by other observers (Anders, Satherthwaite, Curtis and others) that the septic poison, after the destruction of the bacteria, retains its noxious properties. Even injections of putrid liquids, containing bacteria, into the blood of animals, is not always followed by septicæmic symptoms. Thus *Livon*, who injected such liquids into dogs, observed no traces of parasites in the blood, nor any pathological changes in the organs. Davaine found that septicæmic blood loses its virulence by putrefaction, and, moreover, that the blood taken from *living septicæmic* animals had no deleterious effects upon the animals when introduced into the blood.

The micrococcus form of bacteria, besides being met with in the blood and secretions of pyæmic patients, has in a limited number of cases also been observed in diphtheria, especially in the diphtheritic exudate and ulcers, through which, in some instances, they may have found access to the blood; furthermore, in the vesicles or blisters of erysipelas, and even, in exceptional cases, upon the valves of the heart in endocarditis. The experiments and observations relating to the presence and signification of bacteria in the diseases mentioned are very numerous, and the literature of the subject has become too extensive to be thoroughly discussed in this place. Nevertheless, in order to enable the reader to judge for himself, I shall cite the observations and views entertained by some of the leading pathologists. Thus, *Billroth** frequently found cocco-bacteria in the different normal fluids of the body, especially in the serum of the pericardium; but by no means constantly in the blood of the cadaver of persons who had died of septicæmic diseases, even not in the purulent contents of abscesses, etc. The report is as follows:

"The essential cause of their accumulation was most probably here and there the higher or lesser degree of decomposition of the parts. A conditioning relationship of these organisms to the coagulation of the milk, as well as to the alkaline fermentation of the urine cannot be presumed, as they can be demonstrated, here and there, long before the commencement of the process. It is

* *Virchow u. Hirsch*, Jahresbericht f. d. Jahr 1874. Vol. I, p. 353.

known that the pus of ordinary, apparently healthy granulating wounds contains numerous cocco-bacteria; also, that the quantity of those present stands in no definite proportion to the height of the fever or other general phenomena of the patient. In the reverse, cocco-bacteria are found in the pus of closed abscesses without the co-existence of fever, while, on the other hand, in similar cases, high fever may exist without cocco-bacteria being detected in the pus. Finally, the presence of cocco-bacteria cannot arbitrarily be asserted from the bad odor of the pus. A very similar relation exists in erysipelas; while, namely, the serous contents of the blister in half of the cases examined contained no cocco-bacteria, they were found several times under the epiderm' in non-specific exudations."

"All forms of cocco-bacteria may be produced by artificial cultivation from those parasitic forms found in the organism under different pathological conditions, though none of them would, in its different phases of development, show any essential character differing from those bacteria associated with putrefaction. From this it results that not even a specific mode of appearance is observed on the bacteria met with in the animal organism, opposite to those found in inorganic nature. Still less can this be asserted for definite pathological conditions, or for individual diseases."

"The conditions essential to the regular growths of the cocco-bacteria are only partially known and certainly very complicated; the presence of decomposable organic substances is by no means sufficient, which is proved by the want of correspondence between the commencement of putrefaction and the appearance of these organisms, and also by a want of a definite proportion of the quantitative extent of the latter to the putrefaction. The presence of water and air, as well as a certain passivity and undisturbed position of those parts serving as a place for their germination and proliferation, are undoubtedly essential for the development of the organisms. But even then, a further increase in numbers does not take place, as the experiments of Max Wolff have proved, who failed to observe any septic phenomena after the introduction of fungous spores into the trachea, though he could detect the particles in question in the circulating blood. The numerous statements concerning the presence of bacteria in the blood in this

or that disease, also, must be received with great care, as there are other very pronounced cases of septic disease in which they are, at least in entirely fresh blood, certainly wanting. It appears, therefore, that the 'vitality' of the organism exerts a certain conditioning influence upon the destruction, that is, the further growth of the accumulated fungous germs in the circulating blood, as in the secretions and exudations, etc. This fact may be better understood in presuming that the cocco-bacteria are unable to assimilate the albuminous bodies of the tissues in the form in which they exist in the living organism."

"In order that this assimilation may take place, a third hitherto unknown body, which Billroth designates as 'phlogistic zymoïd,' must take part, that is, a body which, produced in the course of the inflammation and by this process itself, excites the fluids of the tissues, the blood, pus, etc., in the way of a ferment, rendering them a suitable and accessible medium for the multiplication of the dormant germs contained in it. This phlogistic zymoïd acts wherever it comes in contact with healthy tissues, but still more rapidly upon diseased tissues, in exciting them to inflammation and causing their destruction. By the disintegration of the tissues thus induced, the ground becomes prepared for the unlimited proliferation of these parasitic vegetations. In speaking of the putrid infection, Billroth declares it very probable that the respective poison arrives in the organism in the form of a finished chemical body, exhibiting its effects in proportion to its respective quantity: a conception standing in opposition to the generally adopted fermentation theory."

"*Panum*,* in continuation of his former investigations concerning the relations of the parasitic organisms to putrid processes, published in 1856, renews the question whether the microscopical organisms contained in the ordinary putrefying liquids, can be regarded as the intermediate cause of that group of symptoms designated putrid or septic infection. As he was unable to deprive, by long continued and energetic boiling, putrid liquids of their noxious properties, by which the vegetable organisms contained therein must necessarily be killed,—he arrived at that time at the conclusion that their deleterious properties could not

* L. c. p. 354.

be ascribed to the micrococci and bacteria, but to another lifeless agent, representing a pure chemical body. Before passing to his more recent experiments, corroborating this view, he endeavors to demonstrate by deduction the improbability of the doctrine, according to which the bacteria are the direct septically acting agents. He mentions the fact, confirmed by Magendie, Gaspard and Stich, that the intestinal canal of healthy men and animals contains an extractible substance, which injected into the blood gives rise to all phenomena of sepsis. The circumstance that the latter do not appear under normal conditions, has been made use of as a proof for the molecular, insoluble nature of the poison. But bodily substances also, even psorosperm-eggs, may pass through the epithelium of the intestine, while many soluble substances, as a solution of curare, for example, pass with extraordinary difficulty. Against this supposition is, furthermore, the fact that the duration of the time of incubation in septic diseases does not stand in the reverse proportion to the quantity of the injected liquid, which certainly should be the case. As regards, finally, the clinical symptoms of the septic infection, Panum finds the characteristic points of the course not in the curve of temperature, but in the affection of the intestine, announced by vomiting and diarrhœa ; then in the severe collapse and depression of the entire nervous system, and finally in the rapid appearance of putrefaction and the imperfectly coagulating blood. From this it is clear that we are not justified in forming from the symptoms of the poison, and especially from the duration of the course of the affection depending upon the dose and the concentration of the injected liquid, an argument for the essential participation of the at the same time introduced microscopical organisms."

"Against the bacteria-theory, the fact that a putrefying liquid, rendered perfectly free and clear from bacteria by repeated and continued filtration, loses nothing of its septic effects, may be most strikingly brought forward. Of the entire absence of bacteria, Panum became convinced by means of high amplifications. By a repetition of the experiments with putrid liquids, which had been boiled for several hours, he became still more convinced that the distillate obtained from it, though of a bad odor, was not poisonous, while the deleterious effect of the residue was little less

than that of the original liquid. The alcoholic extract of the clear filtrate of meat, which had been macerated for four weeks, injected into the blood of a dog, shows only a hypnotic effect. The residue, not extracted by alcohol, however, gives rise to vomiting, inclination to stool, tenesmus, and general depression, from which the animals scarcely recover after the lapse of twenty-four hours. In view of such results, Panum regards it as settled that the putrid poison is no simple extractive substance, but a real chemical body; the latter being the true deleterious agent in the septic processes, while the part of the bacteria is only accidental."

"As regards the origin of this putrid poison, Panum suspects that it is produced by the vital process of the bacteria, perhaps a kind of secretory product (Bergmann). All experience relating to the presence of bacteria in the healthy organism of man, as well as in the diseased, teach us at least that, both bacteria and processes of putrefaction, stand in near relationship to each other. Though, undoubtedly, bacteria also appear in the body with decomposition, their increase always depends upon the cessation of life, be it from local or general causes."

"*Hiller*,* in concert with the results of his former researches, states that in putrefying urine the degree of development of bacteria does not always correspond with the height of the decomposition, but that both rather stand to each other in a reversed proportion. Thus, urine left in an open, or corked, perfectly clean bottle, does not, even after two months, undergo putrefaction; the latter, however, took place in some bottles closed with cotton, and even earlier. Notwithstanding this difference in the results of the experiments, all specimens of urine corresponded in containing a rich vegetation of bacteria after the lapse of only a few days. But this vegetation only attained a certain low degree, and then remained stationary, if afterward a putrid decomposition was not induced. As long as the urine standing open was acid, mycelii of Penicillium glaucum and Torula cerivisiæ would grow, but with the commencement of alkaline reaction, the former disappeared entirely, and the latter partially. As regards the influence exerted by various chemical agents upon the putrefaction, ammonia and carbonate of ammonia remained negative. Phos-

* l. c., p. 365.

phate of potassa and soda, as well as tartrate of ammonia, promoted in a high degree the development of bacteria, without producing putrefaction. Specimens of fresh urine placed in a close vicinity to putrefying urine showed extensive masses of bacteria without putrefaction."

"The putrefaction of urine, therefore, cannot be looked upon as a physiological phenomenon of exchange of matter through the bacteria. The vegetation of the latter depends solely upon the supply of assimilable nutritive matter, which, being scanty in fresh urine, is only furnished in sufficient quantity through the putrefaction. As, now, the bacteria are powerless to split the complicated (nitrogenous) combinations in the urine, it requires, in order to nourish them, an agent that induces the decomposition. This agent becomes active through and with the putrefaction, and from this the coincidence, regarding time and extent, of putrefaction and bacteria may be explained.

"In setting aside the decompositions taking place in the urine, experiments with chicken eggs show moreover that bacteria alone are incapable of inducing a putrefactive decomposition in the albumen. From this Hiller concludes the untenability of the vitalistic theory; he is moreover of opinion that the ferments of putrefaction are represented by most minute proteïn-particles, which, being themselves in a state of putrefaction, are carried through the air to the substratum, to involve it in a similar decomposition."

Although it had been stated by Pasteur, and corroborated by other observers, that no microscopic organisms could be detected in the healthy blood, experiments were nevertheless also made to prove the contrary. Thus, *Tiegel* took pieces of different organs of freshly killed animals, and fastening them to a previously boiled silken thread, plunged them successively into boiling paraffine, until they were covered by a thick layer of this material. Though it was supposed that the boiling heat of the paraffine had destroyed every living germ at the surface of the pieces, and that the layer of paraffine covering them had prevented the access of fresh germs, bacteria were nevertheless found in the interior of the pieces after the lapse of several days.

These experiments, while attracting much attention, were re-

peated by other investigators; and as the results obtained corroborated the statements of Tiegel, it was concluded that the bacteria themselves, being always present in the blood, were unable to exert any influence upon the production of pathological processes *Burdon-Sanderson*, also, investigated this matter, by repeating Tiegel's experiments with a slight modification, rather improving the process; and in referring to the experiment in one of his lectures on "The Infective Process of Disease," delivered in the University of London, about two years ago, he says that under the conditions described it seems to him quite impossible to suppose, either that germs could penetrate to the organ (the liver or kidney) from the outside, or that any germ encountered by the organ in its transference from the body of the animal to the basin could escape destruction. If, therefore, bacteria be found, they or their germs must have been there before the organ was plunged into the hot liquid. From these experiments, he then concludes that germs continually enter the blood by the way of the portal circulation, and as no bacteria exist in the circulating blood, the alternatives are that, either the bacteria are formed and immediately afterwards destroyed, or they are not allowed to germinate, because the conditions under which they are placed in the living organism are such as to prevent their development.

Burdon-Sanderson then fully endorses the correctness of Tiegel's statements, and moreover explains the phenomenon according to his own views. But in looking again at the other side of the question, it will be found that *Chiene* and *Ewart* definitely proved the absence of bacteria or any other organism, if removed and examined under a spray of a solution of carbolic acid, together with other precautionary measures, taken during the experiment to prevent the access of these organisms. From these experiments we may learn to receive the statements regarding the presence of bacteria in the living blood or tissues with a great deal of caution.

The last disease in which bacteria have been obtained by artificial cultivation from the secretions of the animals, is *infectious pneumo-enteritis* of the pig, as it has been termed by **Klein*, who investigated it two years ago. The anatomical changes met

* *Quarterly Journ. of Microscop. Science*. April, 1878.

with in this disease are similar to those already mentioned in connection with splenic fever, consisting principally of lobular pneumonia, ulceration of the mucous membrane of the intestines, the liver, spleen, etc. The results of these experiments showed: 1. That the fresh blood of diseased animals does not, as a rule, contain the virus, as it fails to produce the disease when introduced into a healthy animal. 2. That the fluid as well as the solid lymph of the diseased peritoneum contains the virus in a very active state. 3. That parts of the diseased lung, ulcerated intestines, and diseased spleen contain the virus in a very active state; a frothy, blood-containing matter, found in the trachea and bronchi, also possesses infectious properties, showing that the breath of the diseased animal is charged with poison. 4. That infection is produced by cohabitation with a diseased animal, or by keeping healthy animals in a place whence a diseased animal has been removed

By some other experiments, Klein furthermore showed that the virus may be cultivated artificially outside the body of an animal, as had been successfully done by Koch, in splenic fever.

The cultivation of the virus consisted in taking a minute portion of the lymph, and inoculating a drop of fresh aqueous humor of a rabbit, which, being placed upon a glass-slip and arranged in such a manner as to prevent the access of air, was kept in the incubator for twenty-four hours at a temperature of 33° to 34° C. With a minute portion of this fluid another drop of aqueous humor was inoculated and treated in the same manner; and from the latter a third, representing the third generation. Two animals inoculated with this matter were affected with the disease.

In a similar manner the virus was cultivated from a minute portion of solid lymph of the peritoneum of a diseased animal, and the cultivation carried to a fourth generation. Two animals, having been inoculated with this matter, became smitten with the disease. And, in carrying the cultivation of the virus to the eighth generation, the matter remained still effective.

The microscopical examination of the cultivated liquids showed that they were the seat of the growth and development of a kind of bacterium, resembling Bacillus subtilis of Cohn, and repre-

senting a fine delicate rod, thinner than the Bacillus anthracis of Koch.

The interpretation which Klein gives of the results of his experiments appears to me, for several reasons, not calculated to inspire much confidence. Thus, failing in transferring the disease from one animal to another by the inoculation of the blood, he succeeded with the inoculation of the exuded lymph, showing that the virus really existed in the latter. In this paper he omitted to mention whether he had examined the blood and lymph microscopically, and whether, or not, he had detected bacteria in one or the other; but, as he resorted to artificial cultivation, it may be presumed that he did not. Obtaining at last these organisms with their spores, he looks upon the latter a the true cause of the disease, without explaining whence they came. If they had been the true cause of the disease, they must have originally existed in the blood, from which they might have gotten into the secretions, and Klein should have detected them in this fluid as readily as he discerned them in the cultivated liquid. Besides this, he says: "After many failures—owing to the introduction of *Bacterium termo*—I succeeded at last in obtaining, already in the second generation of original virus, a pure crop of bacillus and its spores." Now, as will be seen, that with the bacillus he also obtained bacterium termo, rendering it very probable that both were derived from the same quarter, that is, from the outside; or, if not, that both, according to Ewart, represented different phases of one and the same organism, and, perhaps, originated in the same manner, as the bacilli in the dead mice and rats of Dr. Timothy Lewis. At any rate Klein did not consider it *impossible* for other organisms to make their appearance in the cultivated liquid, as further on he remarks that "no other organisms appeared in these cultivations," *i. e.*, after the bacillus had displaced the bacterium termo. As regards pneumo-enteritis of the pig, therefore, it is more than probable that the peritoneal exudate itself represents the infectious poison.

In comparing the four diseases above described with each other, we cannot but notice the similarity of their accompanying symptoms, and of the anatomical changes observed after death. They are all characterized by an affection of the spleen, lungs,

heart and intestines, accompanied by hæmorrhages, ecchymoses, and metastatic abcesses, symptoms depending more or less upon a depraved condition of the blood, and resembling those of typhus fever. Therefore, it may be presumed that the presence of living organisms, found in the blood of the affected men and animals during the last stage of these diseases, is due to the diseased condition of this fluid, affording a favorable medium for their development, and that the diseases themselves are due to the introduction of some specific poison into the blood, representing a product of the diseased organism itself.

That organized bodies may exist in the blood of certain animals without interfering with the normal functions of this fluid is sufficiently proved by the discovery of E. Ray Lankester, in 1871, of a large infusorium in the blood of the common frog of Europe, *Rana esculanta*, which he called *Undulina ranarum;* and, furthermore, by my own, made almost at the same time, of a similar infusorium in the blood of our tree-frog during three successive years. Though these infusoria were quite numerous in the blood of these animals, nothing abnormal could be discovered in the blood of the latter, a considerable number of which I kept under observations for many months.

In addition to the experiments and opinions of a number of distinguished pathologists, which, in the preceding pages, I have brought before the reader, I shall, before dismissing the subject, cite some portions of a remarkable address, delivered, in 1875, to the Pathological Society of London, by Prof. H. Charlton Bastian,* the well known advocate of the theory of "Spontaneous Generation," whose persevering studies into the nature of minute living organisms have not been surpassed by any other investigator. In the course of this address he says:

"I will, however, now briefly enumerate the evidence which seems to me quite sufficient to disprove the probability of the existence of any casual relationship between the lower organisms and the diseases cited at the head of this section, and to establish, on the other hand, the position that the bacteria met with in diseased fluids

* The Microscopic Germ-Theory of Disease; being a Discussion of the Relation of Bacteria and Allied Organisms to Virulent Inflammations and Specific Contagious Fevers.—*Monthly Microscop. Journal*, August, 1875.

and tissues are for the most part actual pathological products—that they are, in fact, engendered within the body, or are descendants of organisms owning such an origin, rather than of previously existing organisms introduced from without. It would take too long were I to enter upon a consideration of this evidence. I must therefore content myself with briefly summarizing the principal facts and arguments on which a judgment may be founded."

1. "The experiments of many investigators prove that the alleged causes of diseases may be actually introduced into the blood-vessels of lower animals by thousands without producing any deleterious effects in a large proportion of the cases."

2. "Bacteria, if not actually to be found within the blood-vessels of healthy persons, do nevertheless habitually exist in so many parts of the body in every human being, and in so many of the lower animals, as to make it almost inconceivable that these organisms can be the cause of disease. In support of this statement I have only to say, that even in healthy persons they may be found in myriads in and about the epithelium of the whole alimentary tract from mouth to anus; they exist throughout the air-passages, and may be found in mucus coming from the nasal cavities, as well as in that from minute bronchi. They exist abundantly amongst the epithelial débris within the ducts of the skin, not only in the face, but in the other parts of the body. Fresh legions of them are also being introduced into the alimentary canal with almost every meal that is taken, whence they may, perhaps, readily find their way into the mesenteric glands, if not farther within the system. And, lastly, in persons with open wounds, bacteria are constantly to be found in contact with such surfaces, especially if the wounds are not well cared for, though the injured person does not necessarily suffer at all in general health."

3. "It is no answer to these difficulties to say that there are distinct species among the lower organisms, some of which are harmless, though others are poisonous (or so-called germs of disease). In support of such an opinion nothing can be alleged save some of the facts whose cause is doubtful; whilst against such an interpretation may be brought the experiments of several investi-

gators, showing that bacteria are the creatures of circumstance, and modifiable to an extraordinary degree. The last position is even admitted by Professors Sanderson and Lister. The former acknowledges that they are 'the lowest organisms,' and that they are 'much more under the influence of the conditions under which they originate and are developed, than organisms of any other class;' while Professor Lister's own work has compelled him to make an admission which, in the face of facts previously stated concerning the wide distribution of bacteria within the body, seems fatal to a consistent belief in the germ-theory of disease. He says: 'If the same bacterium may, as a result of varied circumstances, produce in one and the same medium fermentative changes differing so widely from each other, as the formation of lactic acid and that of black pigment in milk, it becomes readily conceivable that the same organism which, under ordinary circumstances may be comparatively harmless, may at other times generate products poisonous to the human economy.'"

4. "The considerations now to be mentioned suffice, in my opinion, to complete the discomfiture of the germ-theory as an explanation of the mode of causation of the disease with which we are at present concerned. It is this. It has been shown, on the one hand, that the virulence of certain contagious mixtures diminishes in direct proportion to the increase of bacteria therein; and on the other hand, it has been equally proved that fresh and actively contagious menstrua lose scarcely any of their contagious or poisonous properties after they have been subjected for a few minutes, when in the moist state, to a temperature which no living units can be shown to survive (212° F.), or after they have been exposed to the influence of boiling alcohol, which is well known to be equally destructive to all recognized forms of living matter. Such facts have been substantiated by Messrs. Lewis and Cunningham, Sanders and others."

"Having said this much in opposition to the germ-theory, let me as briefly enumerate the facts and arguments which seem to me to show the real relations of bacteria and their allies to the diseases in question. I turn therefore to the construction of an opposite doctrine."

"Admitting, in part, the very frequent presence of bacteria in

diseased fluids and tissues, I consider that their presence and import should be differently explained. I say I admit the association in part, though I by no means admit it to the extent alleged. Bacteria are not, for instance, to be found in the blood of persons suffering from pyæmia, as might be inferred from former statements of Dr. Sanderson, which I have already quoted. My own experience in this matter seems to be entirely in accordance with that of Professors Billroth and Stricker. Neither do I believe that the presence of bacteria in inflammatory fluids has the significance which Dr. Sanderson attaches to it, since it has been ascertained by myself and others that the exudation fluid of sick persons suffering from disease of a totally different type are often similarly crowded with these lowest organisms, whilst the recent observations of M. Bergeron seem to show that they may be found even in freshly extracted pus from ordinary abscesses occurring in elderly persons."

"Now, it would seem quite obvious that the consistent advocate of a germ-theory of a disease can only successfully maintain such a doctrine if he can show, amongst other things, that bacteria are more capable of altering the character and chemical constitution of fluids of the body than they are themselves prone to be altered by independently initiated changes taking place in such fluids. It seems, therefore, like unintentionally cutting himself free from the theory to which he has hitherto adhered, when we find Professor Lister, in speaking of the assumed 'special virus of hospital gangrene,' going on to say that 'it is not essential to assume the existence of a special virus at all, but that organisms common to all the sores in the ward may, for aught we know, assume specific properties in the discharges long putrefying under the dressings.' This passage has a similar import to that of a quotation previously made. In both a first plea is assigned to the modifying influence of altered fluids; and however much the correctness of such supposition wonld tell in favor of cleanliness, free exposure, or even of antiseptic dressings, it is none the less inimical to a consistent holding of the theory on which Prof. Lister has chosen to base his system of treatment."

"But though such statements are adverse to the holding of a germ-theory in the only form in which it may be at all tenable,

they are entirely in accordance with my own observations and views. I maintain, in short, that even the very existence of organisms in the fluids and tissues of diseased persons is for the most part referable to the fact that certain changes have previously taken place (by deviation from healthy nutrition) in the constitution and vitality of such fluids and tissues, and that bacteria and allied organisms have appeared therein as pathological products—either by heterogenesis, or by what I have termed archebiosis, or birth direct from a fluid."

"The evidence on which my belief is founded is of this nature: 1. Bacteria and their allies are found in greatest abundance during the life of the individual in connection with dying tissue-elements, and apparently are as plentiful with dying epithelium of the cutaneous ducts, as in parts like the mouth, which are most liable to contamination with organisms from without. Again, they exist abundantly in and about the dying cells of bronchial mucus, although living bacteria appear to be almost completely absent from ordinary air.

"2. The microscopical examination of such epithelial or mucous elements also favors the notion that the contained bacteria are products engendered within such cells rather than mere results of an external contamination and imbibition. This opinion is based upon the following considerations. Bacteria only appear within the cell when it is obviously dying; and in the case of the epithelium, for instance, they manifest themselves at first as minute motionless particles scattered through the semi-solid substance of the cell, where each particle grows into a distinct bacterium, which still remains motionless, and does not appear to divide for a long time. This is precisely similar to what I have observed over and over again, when amœbæ in vegetable infusions get into an unhealthy condition and become resolved into nests of bacteria. They may exist for days in a state of activity with bacteria in the fluid around them, though none are to be seen in their interior. After a time, however, the chemical constitution of the fluid seems to become no longer suited to the amœbæ; their activity ceases, they remain as almost motionless balls of jelly, and soon multitudes of the minutest particles appear throughout their substance, each of which straightway grows into a bacterium. The

former amœba is converted into a mere bag of bacteria, which after a time ruptures, and thus liberates its swarming colony of newly-engendered living units. Multitudes of mucous corpuscles seem to undergo the same kind of change, so that bacterial degeneration takes place in the same manner and is almost as typical amongst them as is fatty degeneration amongst pus-corpuscles. The two kinds of degeneration, moreover, commonly occur side by side in epithelial dèbris. Bacterial degeneration takes place where the vitality of the unity is lowered, but where it is not sufficiently degraded to permit of the still lower and more obviously distinctive process of fatty degeneration; and if any one wishes to see it in perfection let him examine some central portion of the kidney or other internal organ of a warm-blooded animal five days or more after its death."

"3. Bacteria are admitted by nearly all pathologists to be absent from the blood of healthy persons during life, and yet in from eight hours to four or five days after death, according to the temperature of the air at the time, the previously germless blood of individuals may be found to be swarming with these organisms in every stage of growth."

"4. Whereas blister fluid or serum has been shown to be free from organisms in healthy persons, I have ascertained that, given a febrile patient with a temperature of 102° F., one can determine the presence of bacteria, as will, in any blister-bleb which remains intact for forty-eight hours or more, and this, too, when the patient does not suffer from any specific fever, but merely from pneumonic inflammation. I was led to ascertain this fact by finding, about eighteen months ago, myriads of bacteria in all the blebs of a patient suffering from acute pemphigus, with a temperature of 103°."

"5. Lastly, as Dr. Sanderson has shown, a chemical irritant, such as liquor ammoniæ, may be introduced beneath the skin of some of the lower animals in such a way as to 'preclude the possibility of external contamination,' and yet here, amidst tissues which he has shown to be germless, we may thus, within twenty-four hours, determine the presence of swarms of germs and organisms in the pathological fluids effused under the influence of the local chemical irritant."

"This constitutes, as it appears to me, an exceedingly strong body of evidence tending to show that bacteria are pathological products capable of being engendered within the body after death."

The untenability of the germ-theory has been so ably demonstrated by Prof. Bastian in his address as to require no further comment. In explanation of the origin of bacteria in those diseases in which they have been met with in the tissues, he offers his own theory of "heterogenesis" and "archebiosis." In examining and considering this subject more thoroughly and without prejudice it becomes difficult to perceive any impossibility in bacteria arising, at least, by heterogenesis, as Bastian designates that process by which the particles of living tissues, on the eve of the death of the latter, may individualize themselves and continue to live in the form of a low organism. For my own part, I venture to endorse what he says.* "Just as the life of one of the cells of a higher organism may continue for some time after the death of the organism itself, so, in accordance with this latter view, may one of the particles of such a cell be supposed to continue to live after even cell-life is impossible." That cells do live many hours after the death of the animal or man is corroborated by my own observation which I made in 1867—when examining the epithelium of the mucous membrane of the frontal sinuses of a yellow fever patient eleven hours after death—and consisting in the active motion of the cilia of a single epithelial cell, causing a movement of the cell itself, similar to that of an infusorium. The same phenomenon has been observed on ciliated epithelial cells, even at a longer time after death, by other observers. As regards Bastian's theory of archebiosis, it is more difficult to accept it at present, though the fact that there must have been a time in the history of the earth when organic matter arose from inorganic, and in its turn gave rise to the first living organisms, cannot be overcome. The theory of the development of bacteria from putrefying starch granules has been advanced previously to Bastian by *Hartig*, who has even repeated his former assertions. The origin of the minute moving granules found in the vesicles

* *Bastian—The Modes of Origin of Lowest Organisms.* 1871, p. 15.

of variola and vaccina, which *Chauveau* regarded as the carriers of the specific poison, also, would find an easy and reasonable explanation by the heterogenetic theory. We may furthermore refer to the observations of Lewis on dead mice and rats, cited already in the preceding pages; and lastly to some of my own, as follows: In 1867, in examining the brains of yellow fever cases, I put small pieces of the cortex cerebri in small wide-mouthed bottles containing a solution of one-third of alcohol to two-thirds of water. The bottles were filled up to the top, so that when the cork was inserted the liquid would run over, and no air be left within. In examining these pieces four days afterward, I found great numbers of minute organisms in their interior. Some of them represented micrococcus, even zogloæ, and vibrios; but there were others, rod-like forms with highly refractive granules, unknown to me at that time, but which I found afterward explained by the labors of Koch and Ewart. In these cases, however, I shall not preclude the possibility of some of these organisms having adhered to the surface of the brain before they were put into the alcoholic solution.

In drawing a final conclusion from what has been said in the preceding pages upon the bacteria question, we may well presume that they do not represent the direct cause of those diseases with which they have been found associated, unless stronger and more reliable proofs are brought forward in favor of this theory. But, as by this time, in most diseases, the blood and tissues have been examined over and over again by numerous observers, who are anxious, besides, to "find something," without the discovery of other facts than those known for a number of years, it appears quite improbable that this will ever occur.

In order to show that all statements, regarding the presence of minute organisms in the blood and tissues of individuals affected by infectious diseases, must be received with great caution, I shall, before dismissing the theory of the "contagium vivum" in general, cite the views of a few of the most pronounced germ-theorists on the subject. Thus, *Liebermeister*, who theorizes even upon invisible germs, says, more than six years ago:* "It

* Cyclopædia of the Practice of Medicine, edited by Dr. H. v. Ziemssen; American edition, Vol. I.

is true that the triumph of the theory of a contagium vivum is in no way complete, and as in former times, so now, it is not so much its opponents, as it is the imprudent adherents who threaten to bring the theory into discredit. The utter lack of critical discernment and method which have characterized some of the works in this field, and, on the other hand, the recklessness with which facts of uncertain significance have been proclaimed certain proofs, have also in our time driven away many earnest investigators."

Koch,* the discoverer of the spores of Bacillus anthracis, after testifying that "in the blood and tissues of the healthy animal or human organism bacteria are not met with," continues as follows: "It appears to me, however, that the following objections against the acceptation of bacteria being the cause of infectious traumatic diseases are justified. To gain an incontestable proof for this acceptation it is essential *that the bacteria, without exception and in proportions regarding their number and distribution, should be shown in such a manner, as to perfectly explain the symptoms of the respective disease.* For, if in some cases of a certain kind of infectious traumatic disease bacteria are found, while they are absent in other cases exactly alike,—and if, furthermore, the bacteria are present in too small a number as possibly to cause a severe disease or even a fatal issue, it becomes self-evident that their inconstant appearance is dependent upon chance, and their small number no sufficient proof for regarding them as the sole cause of the respective disease, and that we must accept the existence of other causes besides. The observations made in regard to the presence of bacteria in infectious traumatic diseases, however, do in fact not correspond with the demands required for an incontestable proof."

Birch-Hirschfeld,† in speaking of the pathological signification of bacteria makes the following remarks: "But it must be admitted that, even if the constant occurrence of these organisms in the diseases mentioned is recognized as a fact, doubts may yet arise as to whether these bacteria are the real cause of the disease."

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* Koch, R.—Untersuchungen ueber die Ætiologie der Wundinfections-krankheiten Leipzig, 1878, p. 22.

† Birch-Hirschfeld.—Lehrbuch der Pathologischen Anatomie, p. 233.

"This question will not arise with an infectious disease in which organisms of a certain morphological character constantly and exclusively occur, as in recurrent fever, where the spirilla claim a diagnostic signification. In splenic fever this circumstance is less significant."

"The morphological character of the bacteria found in pyæmia, diphtheritis, small-pox, cholera, however, are so much the same, as to give rise to the idea that they are identical forms. But the conclusion drawn from this would be that no specific signification could be assigned to these organisms. Accordingly, they would not represent the cause but parasites of the disease, which, even then, may not be without signification, or may stand in some relationship with certain septic conditions of some infectious diseases."

After the preceding discussion of the so-called "bacteria theory" and of those diseases in which these minute organisms are really met with in the blood and tissues of many cases, we are now ready to inquire *whether this theory may in any way be applicable to yellow fever;* and, in order to arrive at correct conclusions from such an inquiry, it becomes essential that we should set aside all postulation, such as the existence of "invisible" living germs, and strictly keep to observed positive or negative facts. It is self-evident, therefore, that the assertion of bacteria or their spores being the cause of yellow fever must be substantiated by the ocular demonstrations of these organisms in the fresh blood of the patient, before it can be received as a truth. Judging from my own numerous examinations of yellow fever blood under various conditions, already mentioned in this treatise, I need not hesitate to say that this has been done. And, since the results which I repeatedly obtained ever since the yellow fever epidemic of 1867, have now been corroborated by those of *Sternberg*, who, during 1879, examined quite a number of specimens of fresh yellow fever blood at Havana, I may add that all statements to the contrary must have been founded upon an imperfect and inexact manner of microscopical examination. And as, furthermore, bacteria are neither met with in the tissues and organs of fatal cases of yellow fever after death, if properly prepared while still in a fresh condition, we are justified in pre-

suming without further extending the argument, *that yellow fever does not depend upon the presence of bacteria or any other minute living organisms in the blood or tissues*, for, if it did, *the microscope would most certainly show them*, as well as it has done in those other particular diseases mentioned.

But, it will now be asked, if the cause of yellow fever is not represented by minute living organisms, what is it then? And there are many persons, both physicians and laymen, who will promptly answer this question by referring the cause to the products of vegetable and animal decomposition in the form of filth and dirt in the streets and houses. But before I shall attempt to show that the "filth-theory" has no better foundation than the "living-germ-theory," it becomes necessary that I should properly define the standpoint from which I view the subject, as otherwise I might be looked upon as an advocate of dirt and filth. There is hardly a physician who does not consider a supply of fresh and pure air and water as the cardinal objects in public and private hygiene; nor have I, myself, ever regarded these elements in any other light. On the contrary, the degree of civilization of a community may rightly be judged from the degree of neatness and cleanliness of the houses and streets; and nobody will doubt but that the hygienic condition of a community depends to a considerable extent upon the purity of the air breathed by the people in their dwelling-places. It is also true that some local affections may arise from the breathing of air contaminated by gases arising from privies, or from other animal and vegetable decomposition. Such cases may occur in any large city, though not very often; but, that a *specific* and *contagious* disease, characterized by *specific symptoms and pathological changes in the tissues and organs*, should take its origin from such a cause is contrary to all modern scientific knowledge. A specific disease can only be caused by a specific poison; and though certain pathological processes may equally take place in different specific diseases, yet each of the latter maintains its own specific character besides. The poison of yellow fever will never produce scarlatina, and the poison of the latter will never give rise to yellow fever, though in both diseases parenchymatous degeneration of the kidneys may be met with. The development

of a specific disease may be compared with that of the egg; for a certain mysterious agency—similar to that determining the specific characters of an animal or plant, and lying dormant in the protoplasm of the egg-cell—also resides in the poison of a specific disease, determining the specificity of its symptoms and pathological changes. And, accordingly, the inquiry into the origin of these specific poisons will be as resultless as that into the origin of the first egg. As far as I am able to judge, it appears to me that specific diseases have never sprung suddenly into existence, but that their origin must be compared to that of vegetable and animal species, and that, throughout an immense length of time, they have been developed into what they are now by the processes of "selection" and "adaptation." Thus, small-pox, or yellow fever, may have presented a different character thousands of years ago, from what they do at present.

Yellow fever, therefore, being a specific disease, cannot arise spontaneously through the influence of the air rendered impure by the products of vegetable and animal decomposition, for, if this were true, New Orleans would be depopulated long ago. From all I know, the disease, in this city, has never arisen at the outskirts, or in the vicinity of those places to which the kitchen refuse and rubbish of the houses used to be carried not many years ago, or of grave-yards, such as the Locust Grove Cemetery of bad repute, but, on the contrary, always in the populated commercial centers, or in the vicinity of the harbor. Besides, it is a historical fact that this disease almost always first appears in a sea-port, before it extends into the interior of the country, and that it stands in close relationship with the shipping over sea. If yellow fever could ever have originated from the gases arising from decomposing matter, it should have certainly done so in the vicinity of one of those so-called dumping grounds, a large empty lot, situated, not many years ago, on Broad Street Canal between St. Anne and Dumaine Street, and which, in the pursuit of my practice, I had frequent occasion to pass. Whenever I passed, I found it occupied by quite a number of negro rag-pickers of both sexes, accompanied by their dogs, and engaged in digging the ground in search of lost treasures. The stench arising from this place was so offensive and sickening in character that I had to

rouse my horse and hold my breath until I had passed the whole square. In the same way I have frequently met with offensive odors, though differing in character from that of the garbage, arising from the stagnant water of the canal itself, yet I never heard of yellow fever originating in that vicinity, nor did I learn that other diseases prevailed to a greater extent there than elsewhere. As regards the spontaneous origin of diseases in the vicinity of the grave-yards in the city, I need only point to the report of a committee, appointed by the Medical and Surgical Association of New Orleans, for the investigation of this matter, and which answered the question in the negative. Many other instances might be adduced to show that no relation exists between the origin of yellow fever and the filthy condition of some of the streets of New Orleans, or any other city. With this assertion, however, I by no means advocate the existence of grave-yards in the heart of the city, or bad drainage and muddy and filthy streets and houses, for there remains no doubt but that whenever the the disease has once been introduced and assumed the character of an epidemic, nothing will contribute more to it being fostered and propagated than filth and insufficient ventilation. This I know from experience.

It has also been asserted that yellow fever was caused by gases arising from the bilge-water in the hold of the ships, and the latter has even been regarded by some germ theorists as the medium by which the "contagium vivum" was transmitted from port to port. As regards the gases emitted from foul bilge-water, the remarks made on filth and dirt will be equally applicable to this liquid; but, as concerns the living germs which it is supposed to contain, the supporters of such a theory seem to have forgotten that these minute organisms are all inhabitants of the water or other liquids, which they are incapable of leaving except by evaporation; for. minute as they are, they are still too heavy to be lifted out of the liquid with the molecules constituting its vapors, while in a dry condition they may be carried about by the slightest current of air.

Besides the reasons I have given above for showing the futility of the theory of yellow fever originating in filth, or from the gaseous products of decomposing matter, I might still further

enlarge upon this subject,—a subject which, by having been treated so often and so extensively, both in medical and public literature, is now too well known to require any further comment on my part. Nevertheless, in support of my own views, I cannot forbear to cite the views of two distinguished germ-theorists before dismissing it. Thus, Liebermeister* says: "Not a very long time ago it was almost universally accepted that merely the coincidence of certain especial conditions were necessary to cause the autochthonous appearance of certain infectious diseases. As early as the time of the Athenian plague, Diodorus found a sufficient explanation for the origin of the disease in the circumstance that a great multitude of people from all quarters streamed into the city, and, being cramped for room, breathed a corrupted air; "thus they were attacked with disease in an inexplicable manner." How many thousand times since then have medical and non-medical writers pictured social squalor, decomposing filth, unfavorable weather, etc., as the cause of disease! And physicians and laymen were accustomed to take it for granted that the plague and similar severe epidemics originated after this fashion. Many physicians found no difficulty in explaining the origin of syphilis from the mingling and concentration of the immoral elements of numerous nations. The plague arose from the imperfect burial of human corpses, with the consequent corruption of the air; yellow fever originated from foul bilge-water or from crowding of men together in slave ships; typhus fever from the crowding together of persons in badly ventilated dwellings, or from hunger; the cholera from rotten or unripe vegetable food; the typhoid fever from the exhalations of putrid excrements, etc. For many it was an interesting spectacle to realize how the great regulatory operations of nature should be so simple and easily understood, and how every considerable deviation from a proper observation of hygienic laws should immediately be punished by the production of a particular disease. In recent times the standpoint has been essentially changed. The potency of the factors in the *extension* of the diseases in question is not questioned; on the contrary, our knowledge of it has become

* v. *Ziemssen*, "Cyclopædia of Practice of Medicine," Vol. I, p. 17.

more reliable and exact. We have learned, however, that the diseases do not *originate* in this way. It was observed that the battle-fields of Inkermann, strewed with corpses, whose stench drove the armies away, produced no pestilence. We have been convinced that, in spite of the prophecies and premature results, the investment of Metz was never able to produce a single case of typhus fever, inside or outside of the city, or to transform typhoid fever, which prevails there so frequently, to a possibly higher potency, *i. e.*, to typhus fever. We have gradually reached the conclusion that it is only where the specific germ of the disease exists by itself, or has been introduced, that those anti-hygienic factors become active and may then be capable of occasioning an enormous extension of the disease. The germ, however, is not produced by spontaneous generation."

"In fact, at the present time the acceptance of an autochthonous origin for syphilis is, for most physicians, as great an absurdity even as the origin of scabies or of lumbricoid worms by spontaneous generation. It is unanimously said of the plague, cholera, and yellow fever, that they never arise spontaneously, at least on European soil. The spontaneous origin of small-pox, measles and scarlet fever could hardly find a defender now. Perhaps the time is not far distant, when the doctrine of the spontaneous origin of typhoid fever, dysentery, typhus fever, etc., will be universally rejected."

Naegeli, from whose work on "The Lower Fungi and Their Relation to Infectious Diseases," I have already quoted in this section, speaks of the influence of the air upon these diseases as follows: "The air, containing bad smelling or other gases, though disagreeable, is not rendered noxious by it, particularly with regard to infectious diseases. With it, however, the different forms of more or less dangerous cleft-fungi, suspended in the dust-like masses, may be introduced into the body."

"The infected air itself is odorless. A putrefying substance only becomes dangerous after it has become dry, and the bad odor has disappeared. The miasms and contagia are also imperceptible for the organ of smell."

"The microscopical and chemical examination of the residue of filtered air teaches us nothing as regards its noxiousness, as

the infectious matters cannot be distinguished. It will be impossible to pass a judgment upon the infectious nature of any air, before we are able to test the effects of this residue in an experimental manner."

"It is impossible to render infected air innoxious, as it cannot be made free from dust. At the utmost, the dust suspended in the air of an inclosed space may be removed by the vapor of water, or by sprinkling the walls."

By some the origin of yellow fever, as well as that of other diseases, has even been referred to our drinking water becoming pregnant with decomposing vegetable matter while standing in the over-ground cisterns. I shall once more draw from Naegeli's work and cite this author's opinion on this subject. He says: "The drinking water (from wells, rivers, ponds, lakes, groundwater), even if not clean, is not deleterious to health (provided poisons do not get accidentally into it), and, least of all, causes infectious diseases, as those substances rendering it unclean are generally harmless in their nature; the fungi of putrefaction and putrid substances, as well as miasma-fungi, which it contains, represent so small a quantity, as to reduce the probability of a contagion to an imperceptible minimum."

"With this corresponds the experience, which shows that the continual eating of large quantities of humus substances and products of putrefaction, as are contained in foul drinking water, as well as the exclusive and constant use of the latter by whole populations, are without deleterious hygienic effects. A critical consideration of the known facts relating to the spread of infectious diseases, also, shows that contagion has been wrongly ascribed to the water."

The idea that the air we breathe is pregnant with fungus spores and bacteria, and that hundreds of these minute organisms are inhaled with every inspiration, seems to prevail among a number of medical men; and it is this coarse error which has rendered the germ-theory so acceptable to the medical practitioner. It is true that under certain conditions these minute organisms are met with in the air, though in a comparatively small number, for the reason that the natural media in which they live are fluids in a certain state of decomposition, in which they multiply to

countless numbers. Their comparative scarcity in the air has been satisfactorily proved by the observations of *Cunningham*, made some years ago at Calcutta, for the purpose of determining whether there existed any definite relation between the quantity of organic matter in the air and the prevailing diseases, such as diarrhœa, dysentery, cholera, miasmatic fever and dengue, or whether these diseases depended upon certain forms of organisms suspended in the surrounding air. For this purpose he used a weather-vane in the form of a tube, containing a plate of glass covered with a layer of glycerine, to which all particles contained in the surrounding air would adhere. The apparatus was placed in the vicinity of a prison and five feet above the ground. The matter adhering to the glycerine consisted of particles of silica, amorphous granules, carbon, lime, starch granules, cells, hair, fragments of vegetable tissue, filaments of cotton, hairs of insects, oil globules, pollen granules, spores and cells of fungi and algae, sometimes also bacteria, but in a small number. It was impossible to show a relationship existing between the amount of these particles and the diseases above mentioned.

In New Orleans, where rain-water, collected from the roofs of the houses into over-ground cisterns, is used for drinking or cooking purposes, similar objects are frequently found in the water, especially after a long draught, when the dust floating in the air has had sufficient time to settle upon the roofs of the houses. But I have never heard that diseases have arisen from the drinking of the cistern-water containing these miscellaneous particles, except, perhaps, when the water had been standing for a long time in an old foul cistern,—and even then such an occurrence would be very improbable. On the contrary, our drinking water is the purest that could be anywhere obtained, especially after being filtered, as it is in reality distilled water, in the place of which it is also generally used by the apothecaries. I have been using this water now for many years in my microscopical examinations, but I do not remember ever to have met with bacteria in it, though, if used unfiltered, minute fragments of vegetable tissue or other particles may be met with. Bacteria do not appear until putrefaction has set in.

A number of times I have had to listen to the remarks of

medical friends that living germs might exist in the air, too minute to be seen by the aid of the microscope. To this I can only reply that the modern "germ-theory" has not been based upon "invisible" germs. Even Hallier and Pasteur, the most persevering germ-theorists, never attempted to substantiate their assertions by things they could not see. They only failed in proving that the germs or organisms which they did see represented the true cause of disease. The smallest organisms known at present are the monads, bacteria and vibrios, representing minute granules, either single or arranged in rows, as already mentioned. But minute as they are, they really require no high amplification to be perceived in the form of a dot; it is only for the study of their details that high magnifying glasses and correct illumination are required. And, as stated before, the modes in which they multiply have even been studied by the aid of the microscope. The modern microscope is fully able to show things much smaller than these organisms, regarded by the germ-theorists as the cause of the disease; and, unstable as the germ-theory may be, it is surely not based upon imaginary objects. Its failure only consists in its inapplicability to the phenomena associated with the pathological processes of the disease in question.

In the preceding pages I have endeavored to demonstrate that the cause of yellow fever cannot be assigned to the noxious influence of bacteria in the air, for the potent reason *that they are not met with in the blood and tissues* of yellow fever patients, either before or after death. Neither can it be assigned to the noxious effects of the breathing of air contaminated by the products of vegetable or animal decomposition, or to foul drinking water, for such a supposition would be, as I have endeavored to show, in opposition to all experience of modern science, teaching that infectious diseases never arise from these last mentioned causes. There is, however, another "invisible" agent left, to the noxious influence and effects of which all the characteristic features of the disease may be referred. This agent represents a certain specific noxious poison, *being a product of the diseased organism itself*, and, in consequence, *of animal origin*. To show the probabilities of this supposition, and to explain the more than

probable manner in which this poison is reproduced and increased in quantity, as well as transmitted from individual to individual, will be our next task.

When, in 1867, the yellow fever appeared again at New Orleans, and soon extended over the city in the form of an epidemic, I adopted the view then generally entertained by the larger portion of the medical profession and the people of this city, that the disease was non-contagious; and as the fungi-theory, originating in the statements of Klob and Hallier, was then prevailing among medical men, I also inclined to the view that yellow fever depended upon some kind of micrococcus floating in the air. And, in accordance with this idea, I examined the mucous membrane of the alimentary canal and respiratory passages in quite a number of cases at the Charity Hospital, but without discovering any micrococci or other minute organisms in those localities; in the same way I failed to discover anything abnormal in several specimens of blood from hæmorrhages of the nose occurring in some of my private patients, or from specimens taken from the dead body at the Charity Hospital. It was only in the black vomit, as already mentioned, that I met with fungi and their spores. But as it was obvious that the organisms contained in this fluid could not have any relationship with the primary cause of the disease, I did not hesitate to discard the fungi-theory, while retaining the view of the non-contagiousness of the disease. And, in view of the analogy certainly existing between some of the symptoms of miasmatic and yellow fever, I became inclined to regard the latter as a miasmatic disease in the most intense degree, depending upon a poison arising from a combination of decomposing vegetable and animal matters. A reason for this view was that the disease principally prevailed in cities in which large numbers of men and animals lived in close proximity along the borders of swampy rivers. This view, which is still entertained by a number of physicians, I favored until the yellow fever epidemic of 1878 made its appearance.

Previous to this time my studies had been principally directed to the pathology and treatment of the disease; and, I must confess that, since I failed to demonstrate the primary cause of yellow fever upon the theory of a *contagium vivum*, I had

paid but little attention to this subject afterward. But when I observed, during this last epidemic, the disease slowly extending, frequently from house to house—and, in many instances, after having once entered a house or a family, not leaving it until it had attacked every inmate who had not been affected by it before,—when I saw it traveling from one district of the city to another, new centers of infection arising in places to which the poison had evidently been carried; and when the epidemic slowly extended from our city to neighboring communities—especially along the railways and other routes of public travel,—even to villages and plantations in the country, my attention was again directed to its cause, and by subsequent and more systematic studies and observations I became convinced of its contagious nature.

It would be impracticable to enlarge upon this subject in this place by citing and discussing individually the numerous cases and instances which speak in favor of the contagiousness of this disease, I therefore only refer the reader to the innumerable reports, both of ancient and recent date, containing the history and statistics of yellow fever. I may, however, remark that any physician who will take the trouble and devote the time to an impartial and philosophical study of the subject in all its details, following the outlines which I have sketched in this treatise, will finally become convinced, like myself, of the contagious nature of this disease. My own observations and studies have even inclined me to regard the infectious poison of the latter as more subtile and virulent in its nature than that producing small-pox.

Yellow fever, then, is a disease, running a regular course, and accordingly depending, like small-pox, scarlet fever, measles, and other kindred diseases, upon a specific poison of animal origin, being a product of the diseased human organism itself. This assertion is proved by the characteristic feature which it presents in common with all other specific diseases, consisting in the *immunity* from a second attack, imparted to the individual once affected; and this immunity from a second attack, which most strikingly distinguishes contagious diseases from all others, must be constantly kept in view in the study of the nature of the peculiar poison producing yellow fever.

The precise nature of the particular pathological changes which impart to the organism this immunity from the effects of the poison afterward, we are at present unable to determine. Perhaps the most popular view is that the poison alters the constitution of the blood in such a manner, and so permanently, as to be unable to make any further impression upon it afterward. It is equally difficult to say whether the changes are wrought upon the colored blood corpuscles in particular, or upon the plasmatic portion, the liquor sanguinis furnishing the nutriment to the organs and tissues of the body. Judging from the unusually rapid disturbance in the nutrition of the organism, manifested by the phenomenon of fatty infiltration and degeneration in a number of organs, and by the nervous disorders, the liquid portion of the blood would appear to be first affected ; while, on the other hand, the facility with which the blood corpuscles seem to part with their hæmoglobin, as my observations have shown, indicates that these bodies must be likewise affected. For a number of years I have, in relation to the difference existing in the impression of the poison upon the blood in miasmatic and yellow fever, been in the habit of illustrating it in a somewhat homely manner by assuming that in the former the impression of the poison is only functional in character, and in consequence evanescent, while in the latter it is organic in its nature, and therefore permanent, and insuring the immunity from a second attack. But, though it appears to me possible that the immunity may depend upon certain permanent changes wrought by the poison upon the blood—difficult as it may be to explain—I cannot forbear to presume that similar changes may at the same time take place in the nervous tissues, rendering them in the same manner unimpressible for another attack.

Besides the immunity from a second attack, characterizing yellow fever as a disease produced by a specific poison, the clinical symptoms, and, moreover, the anatomical changes observed after death, also speak for its peculiar and specific character. But as a specific disease cannot be produced in the human body by a general cause. it is obvious that the specific poison producing it must be derived from another human body affected by the same poison, and that this poison must, necessarily be a product of the

organism of the affected individual. We may, therefore, presume that a *general* cause cannot produce a specific disease.

Yellow fever, when it first appears, never attacks a number of persons isolated from each other at one and the same time, but always, like every other contagious disease, starts from single centers, represented by the infected individuals; and the only manner in which it spreads is either directly from individual to neighboring individual, or indirectly, when the poison, emanating from the affected individual and adhering to clothes and other objects, is carried to a distant place and inhaled by another person. A number of centers may thus arise in different localities of a city, which, increasing in dimensions, may at last meet. In this manner, alone, the infectious poison is able to extend over a large city like New Orleans; and the surest proof of this assertion is offered by the slow march in which the disease walked over our city during the last epidemic. A purely infectious poison, on the contrary, being contained and distributed throughout the air of a city or locality, whether in the form of living organisms, or in the form of vegetable or animal effluvia arising from decomposing matter, will necessarily affect every person susceptible to infection nearly at the same time, and, in consequence, rapidly extend over a city or district. For this reason, the theory of a contagium vivum, or of the miasmatic or effluvial origin of yellow fever, is entirely inconsistent with the contagious character of the disease. But notwithstanding these existing circumstances, there are still a number of physicians who, while they recognize the contagiousness of yellow fever, entertain at the same time the incongruous idea that the cause of the disease is represented by minute living organisms, and for the sole reason, as they say, that this is the only theory upon which they can understand the increase of the poison, as nothing could spontaneously increase unless it were endowed with life.

I shall try to explain this subject by a suitable comparison. In every organized body, whether plant or animal, we meet with an albuminous substance which is regarded as the basis of life, and is generally known by the name of "protoplasm." This protoplasm, as we all know, forms the basis of all tissues performing a vital function, whether consisting of cells or fibers;

and though it is not an organized body, it nevertheless represents living matter and is endowed with the power of appropriating other matter unlike itself—such as the nutritive matters derived from the food and contained in the blood,—and of imparting to it its own properties; or, in other words, of converting this matter into protoplasm. Now, it is upon this principle that all tissues and organs of the body not only rejuvenate themselves, but also increase in size. Thus, the protoplasm of a muscular fiber appropriates new matter and converts it into muscular fiber; the protoplasm of a ganglion-cell imparts its properties to the same new matter furnished by the plasma of the blood, and converts it into nervous tissue, etc. The new matter is in all cases the same, but it is the protoplasm of each particular tissue which represents the converting agency.

The specific poison, having entered the circulation, and being diffused throughout the blood, imparts, like the protoplasm, its own properties to this fluid, giving rise to all the pathological phenomena characterizing the disease. Still, it must be remembered, that the degree of intensity of the disease depends entirely upon the quantity of the poison taken up by the blood. If the quantity is sufficiently large to affect all the blood circulating through the body, the disturbance of nutrition would be so great as to interfere at once with all the vital functions, and the case would prove fatal very rapidly. We may, therefore, presume that, with some rare exceptions, in all cases of yellow fever the poison only affects a smaller or large portion of the blood, leaving to this fluid sufficient integrity to nourish the tissues and organs at least for some days, thus affording an opportunity to the organism to rid itself of the poison. This, however, can be accomplished in no other way than by means of the action of secreting, or, as we may say in this case, excreting cells, the same organs through which the organism rids itself of all other foreign or wasted matter. Thus, the poison, already increased in quantity by that portion of the blood to which it imparted its own properties, is absorbed from this fluid by the cells of different glandular organs during its passage through the capillaries surrounding the individual minute glands. And, in passing through these cells, it again increases in quantity *by imparting*

its noxious properties to their natural secretion, together with which it is finally eliminated from the organism. In yellow fever therefore, as in all other contagious diseases, it is in the secretions, especially those of the glandular cells of the skin and of the respiratory passages, that the noxious poison is contained, and with which it is removed from the system.

In some contagious diseases, the poison, before leaving the body, gives rise to certain pathological processes in the epidermic cells of the skin, manifested by divers exanthematous eruptions, which, in some instances, as in small-pox or the cow-pox, proceed to the formation of vesicles and pustules containing the poison in liquid form. Nevertheless, even in these affections, a portion of the poison leaves the body in a gaseous or vapor form, possessing the same virulent properties as the liquid contained in the vesicles or pustules. In yellow fever the poison emanates from the affected individual only in a vapor form, in which it may be communicated to another individual, or may adhere to surrounding objects, as clothes, bedding, furniture, etc. In the latter case, however, it may be supposed that while adhering to these objects it undergoes a certain condensation by drying, and in which state it is transported to distant places. But, as soon as acted upon by a certain degree of moisture and heat, it again assumes the vapor form in which it may be communicated to other persons.

In holding the view of the contagium of yellow fever or other contagious diseases being transmitted from one person to another through the vapor arising from the secretions of the skin and lungs, we need not presume that the whole vapor represented the noxious poison; on the contrary, we may concur with the opinion of Hiller, already cited, namely, that the ferments of putrefaction are represented by most minute proteïn-particles, which, being themselves in a state of putrefaction, are carried through the air to the substratum to involve it in a similar decomposition. In the case of yellow fever, therefore, these proteïn-particles may be derived from the protoplasm of disintegrated epithelial cells of the glands of the skin to which the properties of the specific poison had already been imparted, and which, on their part, if entering the blood of another individual, are also capable of im-

parting these properties to the constituents of this fluid. This explanation corresponds with the theory that only solid bodies are capable of acting as ferments. Accordingly, the spread of the disease would be affected by the expansion of the vapor of the cutaneous secretion containing these particles into the air surrounding the patient, and inhaled by other individuals—and, furthermore, by the secretion adhering to the clothes and bedding of the patient, or to other neighboring objects; if the perspiration be profuse, as is generally the case, it will also be absorbed by the clothes and bedding.

In yellow fever as in small-pox the secretions of the skin are generally associated, as already remarked, with a peculiar odor. Whether this odor really represents the noxious principle, or whether, being somewhat ammoniacal in character, it is due to the decomposition of urea contained in the secretion, I will not pretend to determine. But, judging from its strength as it emanates from a single patient in a badly ventilated sick-room, we may form an idea of the facility with which the vapor, pregnant with the poisonous principle, may adhere to the clothes of visitors to be carried to distant places, or how easily it may communicate itself through the open windows to neighboring houses and people. But, in order to decide upon the probability of this mode of propagation of the noxious poison of contagious diseases, we should compare it with the manner in which odorous bodies impart their odor to the surrounding air, or to neighboring objects. Although nothing definite is known of the manner in which odors are diffused, or of the nature of the impression which they make upon the ultimate terminations of the olfactory nerves, it is nevertheless supposed (Cloquet),* "that many bodies possess the property of setting free from their substance exceedingly fine particles, forming a kind of atmosphere around the odoriferous body and becoming diffused into the surrounding air; their density diminishes in proportion to their distance from the odoriferous body. Accordingly, the air represents the medium by which odorous substances are spread."

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* *v. Vintschgau*,—"Physiologie des Geruchssinnes"—Handbuch der Phisiologie, herausgegeben von Dr. L. Hermann, Vol. III, part 2, p. 161, 1880. (Still under publication.)

"*Cloquet*, *Bidder*, *Valentin*, *Longet*, and *Poinsot** have mentioned a number of conditions under which the odor is developed. There are, namely, odoriferous bodies the substance of which is incessantly, either partially or entirely, volatilized, while others only became odoriferous under certain circumstances. There are, for instance, plants which exhale only during daytime, or only during the night, or, even, only in the morning. Some plants emit odor when they are dried; a generally known example of this is found in freshly cut hay. Aromatic herbs possess in the dried condition only a feeble odor, but smell tolerably strong when moistened. Bituminous substances have no odor in the dry condition, but a distinct one when damp. The dampness appears, therefore, to favor the emanation of the odor, and still more, if the evaporation is supported by a moderate temperature; heat destroys the odor, and a low temperature arrests its emanation; these lower limits differ with different substances."

"*Liégeois* arrived at the conclusion that minute particles are constantly diffused from the odoriferous bodies, especially when they are in contact with water, in the atmosphere, and arriving at the Scheiderian membrane with the olfactory organ."

From these citations, then, we find that odors are produced by minute particles emanating from the odoriferous body to become diffused throughout the atmosphere, and their emanation is favored by dampness, especially at a moderate temperature. But there are also bodies of vegetable and animal origin which emit no odor, and yet manifest the same phenomena indicating the emanation of fine particles as from the odoriferous bodies. It is, therefore, not essential that a substance, in order to emit or set free minute particles, should be odoriferous. The tenacity with which odoriferous particles adhere to other bodies, especially such of a loose or spongy texture, is very great, so that in some instances it is almost impossible to destroy the odor without the aid of water or chemical re-agents. The numerous examples of this kind, such as musk, castor, the secretion of the odoriferous glands of the pole-cat, assafœtida, etc., are sufficiently known as to require no further comment. It is only to the odor of the

* l. c.—p. 262.

exhalations from the human skin, and to the tenacity with which the minute particles—emanating from the respective secretions from which the odor proceeds—must adhere to neighboring objects, that I wish to direct the attention. The most striking example of this kind is afforded by the dog tracing the trail of his master, or that of another animal in hunting. Many of the most remarkable instances are known and authenticated, in which dogs have traced the trail of their masters to great distances, even into neighboring countries, and which evidently show that a portion of the odorous particles contained in the exhalations of the master, must remain suspended in the air near the ground over which the trail passes, or adhere to the ground itself, notwithstanding the currents of air almost constantly present in the open streets or country. Nothing interrupts the trail but running water, which washes the particles away. In this instance, of course, the olfactory sense of the dog, perceiving these particles, is much more acute than that of man; this, however, does not invalidate the argument, as the particles must be there in order to leave an impression upon the dog's olfactory organ. Still more remarkable is the olfactory sense of insects, by whatever organ it may be represented, which attracts them to matters, which in many instances, even, possess no apparent odor, whilst they certainly must emit particles diffusing throughout the atmosphere to considerable distances to come into contact with the organs of special sense of these animals. It is a known fact, and one to which I can testify from experience, that in hot weather the odoriferous trail of a full-blooded negro may be perceived by the human olfactory sense for a considerable distance.

How strong and dense the exhalations of healthy persons even are, may easily be judged from the offensive odor of the air of small and closed sleeping rooms, if entered in the morning before they have been ventilated; and the tenacity with which these exhalations will adhere to linen clothes or other garments, may be judged from the smell of those articles after having hung for some time in rooms overcrowded with people, as met with among the indigent classes of society.

Now, if we consider the amount of exhalation emanating from the skin and lungs of a yellow fever patient during the course of

the disease, and moreover characterized by the peculiar odor already referred to, it must be obvious that the atmosphere of the room, even with proper ventilation, must become charged with the poisonous particles contained in the exhalation; and if there are several cases in the same house, the air within must eventually be contaminated with the poison; and attenuated as this poison may be, the particles representing it will surely adhere to surrounding objects, or escape through the open windows to be carried to neighboring houses. And, if we furthermore consider the complex nature of the intercourse kept up by the inhabitants of a large commercial city, like New Orleans, the facility with which a considerable portion of the poison, adhering to the garments of the nearer friends and visitors of a number of patients, will be carried to different places and houses must be easily understood by the philosophically thinking mind. For it cannot be supposed that every man, woman, or child, whose friends are lying sick in their homes with yellow fever, will break off their social and commercial intercourse with the rest of the people. In fact, this intercourse is so complex, and its threads so intricately interwoven, as to render the tracings utterly impossible, even to the sharpest detective, and at the very beginning of an epidemic. The many failures that have occurred in the attempt at tracing the first cases of yellow fever of an epidemic to their true origin are due to this complexity of social and commercial intercourse. But more especially to the fact, that it is almost always the *fatal* cases which first attract the attention of the authorities, while the *milder* ones, not seen by the physician, and perhaps not even recognized or suspected by the patient or his friends, themselves, and constituting the larger number, will get well without any medical aid. But, while the latter may not be noticed, they nevertheless reproduce and spread the noxious poison, as well as those terminating fatally.

In my paper on "The Nature of the Poison of Yellow Fever," published in the *New York Medical Journal*, May, 1879, I expressed the idea that the poison of yellow fever, similar to the virulent poison of putrid substances, increased in intensity with each individual through whom it passes. By a subsequent and more mature reflection, however, I have come to the conclusion

that experience does not prove this supposition, as, otherwise, the intensity of the poison would soon reach a degree at which it would affect every person without regard to their degree of susceptibility—though it is not impossible that the virulence of the poison emanating from some individuals may be higher in degree than that emitted by others. But, even without this supposition, the quantity of poison emanating from any yellow fever patient, and possessing no greater virulence than that which originally entered his system, is sufficient to explain the spread of the disease.

As regards the transmission of the poison of yellow fever by ships from port to port which is, as mentioned before, a historical fact, it seems to me that even here the poison is generally carried by the garments and effects of the sailors or passengers, though I would not venture to deny the possibility of its being transmitted by the cargo, especially if the articles of which it consists had been exposed to the air of an infected locality. If cases of yellow fever have occurred during the journey, then there remains no doubt that the poison was carried by the clothing and baggage.

Regarding the decline and final disappearance of an epidemic of yellow fever, it is very generally believed that the noxious poison is destroyed by frost. The truth of this supposition, however, is only apparent, as it cannot be proved by any positive and reliable facts. On the contrary, it is a fact that, at New Orleans, the epidemics had almost always nearly disappeared when the first frost occurred, and that frequently new cases arise long after the appearance of this meteorological phenomenon. Thus, in the epidemic of 1867, I paid the first visit to my last case on the tenth day of December, a case which, though not proving fatal, was nevertheless a severe one, accompanied with jaundice and extensive hæmorrhages of the lungs, the patient being a foreigner who had arrived at New Orleans about two months before she was attacked by the disease. The same thing happened, as far as I remember, at Memphis and other places situated more northerly than New Orleans, where the disease continued to prevail for some time after the appearance of the frost. Thus, the epidemic always reaches its maximum height a considerable time before frost appears, and there remains no doubt that its decline is

chiefly owing to the decrease of the number of those persons susceptible to the action of the yellow fever poison, but also *to the lower temperature condensing the latter upon the objects to which it has adhered, and interfering with its evaporation, both from these objects and from the bodies of the affected individuals, and thus diminishing the chances of its being inhaled by other persons.* At the same time, the systems of those persons who thus far escaped the disease are reinvigorated with the approach of cooler weather in the month of October. These are, as I suppose, the chief causes to which the decline of the disease may be attributed, though the germ-theorists firmly believe that the frost kills the living germs, representing, as they suppose, the cause of yellow fever.

And to causes reverse to this may be attributed the re-appearance of the disease, especially in the year succeeding that of an epidemic, for it is very obvious *that during an extensive epidemic a considerable portion of the noxious poison must have remained adherent to clothing and to the walls of rooms, etc., as well as to mattresses and other bedding by which it had been absorbed with the perspiration of the patient*, some of which, after having existed during the winter and spring—perhaps unexposed to the atmosphere and light, and in a state of condensation—*may, with the returning heat of the summer, associated with moisture, be again evaporated and resume its activity.* There remains no doubt that in this manner the yellow fever epidemic, occurring in Memphis in 1879, arose from the clothing and effects of yellow fever patients from the epidemic of 1878, as soon as the shoemaker opened his box, in which they had been kept during the winter and spring. In the same manner arose those cases occurring in New Orleans in 1879, which, besides, might have increased in number to assume the form of an epidemic, if the board of health had not isolated them as far as circumstances would permit. All so-called sporadic cases arise in this or a similar manner, and it is by no means improbable that the noxious poison of yellow fever, like that of small-pox, scarlet fever, measles, and other contagious diseases, may seldom become entirely extinct in places which it is accustomed to haunt, but constantly lurk about in dark corners deprived of fresh air, to

resume its activity as soon as exposed to heat and moisture—and that, therefore, its fresh importation by ships is not always a strictly essential condition.

A further proof, however, that cold does not destroy the noxious poison of yellow fever, or of any other contagious disease, may be found in the known fact that low temperatures, on the contrary, preserve all organic substances. And to illustrate this fact we have only to point to the huge cadavers of the mammoth, buried for thousands of years in the ice-fields of Siberia, the flesh of which was so well preserved when discovered by the herdsmen of those icy regions, that they made use of it for feeding their dogs. But even if the cause of yellow fever were represented by living organisms, such as bacteria, it could neither be destroyed or killed by the cold of our winters, nor by a much lower temperature. This has been sufficiently proved by a number of experiments, but most forcibly by *Frisch*,* who exposed bacteria to a temperature as low as 87.5° C., below zero, a condition from which they revived with the thawing of the liquid.

Much has been said and written about certain meteorological conditions required for the activity and propagation of the yellow fever poison, such as a certain amount of moisture in the air together with a continued tropical heat, a deficiency of ozone, etc. Though nothing positive concerning these conditions has thus far been ascertained, I would not deny the probability of such particular conditions; for the fact that yellow fever has assumed the dimensions of extensive epidemics only at shorter or longer periods, while, on the other hand, it has frequently existed it the form of so-called minor epidemics, or been represented only by a few sporadic cases, shows that the same atmospheric conditions are not always present. Neither does the noxious poison, after its absorption into the blood, manifest its activity in the same degree in different persons, a phenomenon to be explained by the different degree of susceptibility which these persons possess to the effects of the poison, depending probably upon the particular state of their constitutions at the time when it is

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* *Virchow u. Hirsch*, Jahresbericht fuer das Jahr, 1877, Vol. I., p. 285.

brought in contact with the latter. Thus we frequently meet with persons who have been exposed in many different ways to the action of the poison during several epidemics without ever being affected, but who, after the lapse of many years, are finally attacked by the disease. This was the case with myself; for while I escaped taking the disease in former epidemics, I became infected in 1878, while I was engaged in examining the blood of living patients at the Charity Hospital, and when, in order to obtain the specimen of blood, I was obliged to remain for some time in very close contact with the patient, thus inhaling his exhalations. In such cases the disease mostly appears in the milder form. Nothing is known of the nature of this singular immunity, whether it is owing to a peculiar constitution of the blood or of the nervous system at the time of exposure. Nevertheless, it has at times been taken hold of by the "non-contagionists," and forwarded as a proof of the non-contagiousness of yellow fever. Such an argument, however, must fall to the ground in considering that the same phenomenon is observed equally as well in scarlet fever, measles, and small-pox, etc., the contagiousness of which is universally acknowledged. Thus, a number of years ago, I attended a little girl about seven years old, affected with confluent small-pox; it was the most severe case of which I ever had charge, for the eruption extended from the face over the whole scalp, almost forming a mask, and was associated with considerable suppuration and a loss of the entire hair. In this case, remarkable as it may appear, the mother of the patient had during the whole course slept with it in the same bed, and the grandmother in the same room, without either of them contracting the disease, while the father by only once approaching the bed, at the time when the pustules were drying, rapidly caught the disease which fully developed upon him. As far as our knowledge extends at present, we are unable to offer any explanation of these contradictory facts, and it appears to me useless to indulge in empty speculations.

Although the customary assertion that native-born or long acclimated persons enjoy immunity from an attack of yellow fever has now been sufficiently proved as unfounded, it cannot be denied that, in most instances, acclimatization greatly ameliorates

the severity of the attack. This is most strikingly observed in unacclimated persons, especially in those who have lived in northern latitudes, beyond the yellow fever zone, and who are generally the first victims to the disease. And it has become a general rule, corroborated by all writers, that the nearer a person has been born and lived to the North Pole, the more liable he is to be attacked by the disease, and the smaller his chances will be for recovery. The fallibility of this assertion, however, has also been shown by our experience during the epidemic of 1878, when the French, Italian, and Spanish population of New Orleans suffered equally as much, *if not more*, from the disease than that of Teutonic or Anglo-Saxon origin; even the Negroes did not remain exempt. Nevertheless, as regards non-acclimated or acclimated persons, it is not improbable that the air of the yellow fever zone may in some essential points differ from that of northern climes, enabling it to exert a certain unknown influence upon the constitution of the blood of those persons who breathe it, adapting it, so to speak, to the yellow fever poison. And to this circumstance it is mainly due that the rate of mortality during the epidemic of 1878 had been proportionately much larger in Memphis, Vicksburg, Holly Springs, and numerous other places, than in New Orleans, or even in other parts of Southern Louisiana. Besides this, the proportion of persons who enjoy an immunity of the disease, by having been previously affected by it, to the whole population, is greater at New Orleans than at the places above mentioned.

TREATMENT.

ALTHOUGH from the facts relating to the clinical phenomena, pathology, and probable nature of the specific poison of yellow fever, which I have presented to the reader in the preceding sections of this treatise, a rational course of treatment may be easily deducted, some additional remarks will be demanded to direct the attention of the practicing physician to certain apparently minor, but really important points.

The most simple method of arresting a disease, produced in a previously healthy organism by the noxious effects of a specific organic poison, would, of course, consist in the neutralization of the latter, inducing a cessation of the pathological processes—if not advanced too far—and a gradual return of the organism to its normal condition. Unfortunately, however, medical science has as yet not discovered the antidote of the yellow fever poison, and we must, therefore, look for another method of treatment, by which we may counteract the effects of the poison, and, moreover, assist in its elimination from the system with as little damage to the patient as possible—a treatment, which, if based upon rational principles, should correspond to the natural efforts which the organism is observed to make in the elimination of other infectious poisons. Numerous examples of this kind are constantly witnessed in the so-called critical sweats, diarrhœa and other discharges, or in the eruptions of some other contagious diseases; for, it would be difficult to prove that these processes, though pathological in character, do not represent the effort and the means by which the unaided organism chiefly rids itself of the foreign intruder, the morbid poison. In taking a simple case of intermittent fever as an example, we meet with many of the phenomena as are witnessed in the first stage of yellow fever, but which, in this instance, will disappear with the termination of the sweating stage. The most rational inference to be drawn from this fact, therefore, is that the poison, or, at least, *the product resulting from its combination with one or the other constituents*

of the organism, is eliminated by a secretory, or rather excretory, process of the glands of the skin, or, perhaps, also by the biliary or urinary secretions. The same phenomenon may be observed in small-pox, when the fever abates with the formation of the vesicles, and ceases as soon as the whole eruption is out. From this assertion, however, it must not be inferred that an excessive secretion of the skin, or of the liver and kidneys, will at once eliminate the poison from the system, but it must be remembered, that every gland can, in its normal condition, only perform a certain fixed amount of labor, proportionate to the quantity of its parenchyma, and that any increase obtained by means of artificial or other abnormal stimulation must be followed by a decrease of the normal amount. Besides, some other points and conditions associated with the febrile process, and incompatible with an excessive secretion, must also be taken into consideration. The secretory functions, therefore, should only be moderately promoted if possible, but never be stimulated to excess. The next object in view is to reduce the elevated temperature to near the normal standard for the special purpose of limiting the disintegration of the albuminous substances, which, as is believed by a number of pathologists, is promoted by an abnormally elevated temperature of the body. The third, and perhaps most important point to be observed, however, is to prevent or to allay every excitement of the nervous system.

In passing a review of the clinical phenomena and the pathological anatomy, we find that in all fatal cases the nervous system takes a most prominent part, and in discussing the general pathology of the disease I have endeavored to clearly demonstrate this fact. And it may safely be pronounced that if the integrity of the nervous organs were not disturbed, the organism, if left to itself, would easily get rid of the poison, and the fatality of the disease be removed. This assertion is fully proved by the thousands of cases which recover without any medical aid. The most dangerous of these nervous disturbances is the hyperæmia of the brain, which, as I have shown, is almost always observed in fatal cases after death. For this reason the physician should never neglect to study the condition of the brain of his patient, from the various nervous phenomena manifesting

themselves during the course of the disease, particularly during the febrile stage, and by the proper therapeutic means and applications endeavor to keep the congestion of this organ confined within safe limits. The first condition, essential to the safety of the patient must, therefore, be *the perfect rest of the mind, as well as of the bod*

To secure the necessary rest of the mind for the patient is in many cases quite a difficult task for the attending physician on account of the pernicious custom, especially prevailing among the working classes, of the female friends and neighbors entering the sick-room, and going to and fro for the pretended purpose of inquiring after the condition of the patient, but in reality from idle curiosity. I doubt not that many a case of yellow fever has terminated fatally for the want of the proper rest of the mind, and the proper nursing at the *proper* time. It usually happens that when there are too many friends the patient is neglected, and will have to pay the cost with his life. For this reason, the physician, after having taken the case in charge, should at once select one or two of the most intelligent and trusty friends, who voluntarily offer, to stay alternately with the patient, day and night, at least until the crisis is over. Much has been said about professional yellow fever nurses. I have never had a great deal of faith in these persons, as they are strangers to the patient, and frequently too meddlesome, imagining that they know better than the physician, and not carrying out his orders very strictly—not infrequently even supplanting them by their own notions. The most reliable nurses are always the nearer relations and friends of the patient, whose sentiments and interests are interwoven with his own. The impression made upon the patient, by seeing strange faces around him, can neither be favorable. In the epidemic of 1867, particularly, I observed the marked importance of conscientious and careful nursing in a number of severe cases, who, attentively nursed by their nearer friends and relations, recovered, while others, surrounded and nursed by strangers, succumbed.

As soon as the first symptoms of the disease appear, therefore, the patient should be confined to bed and made as comfortable as possible, both in body and mind. The physician should con-

tribute to keep up his moral courage by representing to him his case as light as possible, and by explaining the importance of the rest of his mind. Intelligent patients I have usually advised to keep from using their mind at all, but merely vegetate, so to say, in trying to sleep, and to leave all cares to their friends. Regarding the sickroom, it is of the greatest importance that it should be well ventilated, as otherwise, not only the patient, but also those persons who nurse him, will be obliged to breathe his cutaneous exhalations containing the infectious poison. At the same time, however, every direct current of air upon the patient should be scrupulously avoided; he should be lightly covered, but his surface not wantonly exposed.

In discussing the general pathology of the disease, I referred to the probable temporary increase of the biliary functions in the commencement of the disease, and, for this reason, the customary initiation of the treatment by the administration of a mild cathartic, for the purpose of unloading the portal circulation, must be recommended. There are a number of medicines which will answer this purpose. The most popular one in this city, both with physicians and the people, is castor-oil, and, if not rejected by the stomach, answers as well as any other on account of its quick action. A number of physicians administer a dose of calomel, combined with one or the other cathartic, such as jalap, etc. As the calomel produces to a certain extent a bilious stool, this remedy rather appears favorable, especially as we know from the autopsies that in almost all fatal cases the gall-bladder contained a dark brown, tar-like bile. The citrate of magnesia may also be used, though it is frequently rejected by the stomach. Subsequently, in the course of the disease, however, it is better to use an enema instead of the cathartic medicine.

The almost universal custom of giving a hot stimulating foot-bath for the purpose of inviting the blood from the brain to the feet, also, may be of service in the beginning of the disease, but with the necessary caution to be administered after the action of the cathartic, allowing the patient to remain undisturbed afterward. The foot-bath, however, will only prove of advantage in the beginning of the disease.

In order to promote the perspiration, it is customary—at New Orleans—to administer an infusion of orange leaves. These leaves, if possessing diaphoretic properties at all, possess them only in an inferior degree. They are simply used in Louisiana, because they are easily obtained. In the Northern States they would be replaced by "boneset," (Eupatorium perfoliatum), and in Germany by the flowers of "chamomile." And as such infusion, in order to produce a diaphoretic effect, should be administered while hot, but which, in most cases, is neglected, the benefit derived from the orange leaves is only imaginary; even if the cold infusion is taken with the view of allaying the irritation of the stomach. Besides, the administration of hot infusions at a time when the patient suffers already from the excess of heat, both from the weather and the disease, is hardly practicable, as it really contributes nothing to the comfort of the patient. Perhaps one of the most efficient and harmless remedies is the "neutral mixture" with the addition of a little ($\frac{1}{16}$ part) sweet spirits of niter, given in such doses as to keep the skin only in an evenly moist condition, which, however, may be discontinued while the skin remains moist, but resumed as soon as the perspiration ceases, and the skin becomes again dry. This mixture is tolerably well borne by the stomach, whilst the spirit of niter, besides, may slightly stimulate the kidneys. But as with the rise of the fever the thirst of the patient rapidly increases, he finally also refuses this remedy, and demands ice-water, which, if given in proper doses, appears to suit the occasion as well as any article the apothecary could furnish. Unfortunately, however, the thirst of the patient is so great that he loses his self-control, and will fill his stomach with the cold liquid if not interfered with by his nurse; then, small fragments of ice suffered to slowly dissolve in the mouth may answer the purpose.

Aside from the medicines above mentioned there will, in the great majority of cases, be no further demand for others during the remaining part of the course of the disease; henceforth, the physician must concentrate his whole attention upon the study of the clinical phenomena of the case, and upon the close superintendence of the nursing of the patient; and, to accomplish this task properly, he must not limit himself to general directions,

but, moreover, explain to the friends or nurse the importance of closely watching the case. He must, furthermore, take the trouble of *giving them a detailed account of the phenomena which might manifest themselves during his absence*, and what should be done in such event to meet them before he is able to see the patient himself. Yellow fever, as we have seen, is a disease of a rapid course, in which the gravest pathological changes may take place in the space of only a few days, and, if anything at all can safely be done to ameliorate the noxious effects of the poison, it must be done during the febrile stage of the disease.

With the progressive rise of the fever the patient becomes more restless, particularly from the sensation of the increased amount of heat retained within the organism, while at the same time a delirium will gradually set in, slight at first, but generally increasing in violence with the progress of the disease. It is hardly necessary to repeat that the appearance of the delirium indicates the abnormal afflux of blood to the head, and the beginning of the hyperæmia of the brain, which, if passing beyond certain limits, will necessarily cause the death of the patient. Therefore, as soon as the temperature of the scalp commences to rise, applications of cold water should be made to the whole cranium. A towel, twice folded to obtain four layers, and *large enough to cover the whole head*, saturated with ice-water, will answer every purpose. These applications, if conscientiously made and attended to, I regard as the most important point in the whole treatment of the disease, though, if *irregularly* and *carelessly* applied, they will fail in their purpose. In order to avoid all interruption in their applications, there should be two towels in use, one of which to be in the ice-water always ready for application, as soon as the other is removed from the head. The most convenient method for keeping them always cold is to put a large piece of ice in a wash-basin containing just enough water to submerge the towel. In many cases it will be found that the heat of the head is so great as to warm the cold cloth in a few minutes. Though it is a difficult task to keep the head of the patient covered with the wet cloth while he is in a highly restless condition, even laboring under delirium, tossing his head from side to side, and frequently changing his position, yet *it must be*

done, for if omitted during the *height* of the delirium, even for a short time, it may be followed by fatal consequences. It is most important, therefore, that at this period, the patient should never be left alone. The efficacy of these cold applications is proven by the patient becoming more quiet every time a fresh cloth is applied, and by his asking for their renewal, whenever he is in a state of consciousness—even after the febrile stage is over. Great care must be taken in making these applications not *too cold*, which would give rise to the opposite condition of the hyperæmia, a depression of the functions of the brain, no less dangerous than the congestion. For this reason, ice should not be applied directly to the head. To the extent of my observation, ice-water, if properly applied, answers all purposes.

While these ice-water applications serve to keep the hyperæmia of the brain within safe limits, they at the same time reduce the temperature of the body by abstracting a considerable amount of heat by way of the head. With the view of lowering the temperature of the body, it is recommended by many physicians to sponge with cold water, alcohol or any other rapidly evaporating liquid. As I regard the perspiration of the skin as one of the processes by which the poison is eliminated from the body, I have never adopted this practice for fear of putting a check to this process, which itself, by the evaporation taking place, can only promote the discharge of heat from the body. Besides, by indiscriminately exposing the surface of the body to the air, difficult to avoid, the blood-vessels of the skin are apt to contract suddenly and *unevenly*, driving the blood to some interior organ of the body, and increasing there the already existing congestion. It appears to me, therefore, that a cold bath of short duration would even be safer to the patient than the imperfect and unequal abstraction of heat by sponging, as the former, by acting more evenly upon the whole surface of the body, would not only more equally abstract the heat, but also prove a stimulant to the nervous system, especially if followed by a timely reaction of the skin.

For a number of years, now, the cold bath has been very extensively used in febrile diseases, especially in Germany, for the purpose of reducing the temperature of the body. This treatment

is based upon the theory that the fatality of the case depends upon the abnormally augmented heat, giving rise to the disintegration of the albuminous substances, and, moreover, causing the various parenchymatous degenerations. Although the statistics taken from a large number of cases, in which the cold bath was used, compared with others of antecedent times and without the use of the bath, evidently show a considerable decrease in the mortality of these diseases, the theory of the fatality of the case depending upon the high temperature is by no means generally adopted. On the contrary, the beneficial effects of the cold bath are by many pathologists attributed to the stimulation which it affords to the nervous system; and this appears to be the true explanation.

"*Warfwinge* * of Kopenhagen, who not long ago investigated this subject more closely, expresses the opinion that the dangerous influence of a high temperature upon the tissues, and particularly upon the muscular element of the heart, has never been proved, and that, accordingly, the high temperature in infectious diseases is of little significance; but that the real danger consisted in an excessive formation of the specific poison of the disease. The collected 2,239 cases of typhus fever, of which 357, or minus the complicated cases, 230 terminated fatally. Only in one-eighth of these cases the temperature rose in the last days to 40° C. or higher; in the remaining seven-eighths the temperature was 39 to 40, 38 to 39, or even under 38° C. In considering the earlier stages of the disease it was found that in 52.7 per cent. of the fatal cases the temperature never reached 40°, and in two-thirds of the remaining percentage of the latter it was not higher than 40 to 40.4° only in one-sixth 41° were reached or passed. From this Warfwinge concluded that in typhus fever the degree of the degenerate processes in the tissues, as well as the derangement of the functions of the organs and the nervous system, are not at all proportionate to the height of the temperature. And, as in his opinion, it is not proved that the temperature in the interior of the body can be lowered by cold bath, he furthermore concluded that the cold baths exerted but a small influence upon

* *Virchow u. Hirsch,* Jahresbericht Jour. das Jahr, 1878. Vol. I. p. 205.

the course of the disease, and should chiefly be regarded as a stimulus for the nervous system."

Besides, there are other diseases and conditions of the organism, such as tetanus, in which the temperature of the body reaches a very high degree, without promoting the disintegration of the tissues or inducing the parenchymatous degenerations of the organs. Even in febrile diseases the disintegration of the albuminous substances commences, as indicated by the augmentation of urea in the urine, before the elevation of temperature, as has been mentioned before.

Nevertheless, cold baths of *short duration*, and repeated at intervals of time during the hot stage, may prove beneficial in the treatment of yellow fever, if used only for the purpose of stimulating and equalizing the functions of the nervous system; though I think that they require, in order to render them safe to the patient, more care and attention than could be generally bestowed upon the patients during an extensive epidemic, when trusty nurses are comparatively scarce. The manner in which they should be given I will quote from Liebermeister,* who has used them very extensively. It is as follows: "For adult patients the full length cold bath of 68° F., or lower, is to be preferred. The same water can be used for several successive baths for the same patient; the bath-tub remains standing full, and the water, representing about the temperature of the room, answers the purpose without change. The duration of the bath should be about ten minutes. If prolonged beyond that it becomes unpleasant to the patient, and may even prove a damage to him. If feeble persons are much affected by the bath, remaining cold and collapsed for a long time, the duration should be reduced to seven, or even to five minutes. A short cold bath like this will have a much better effect than a longer one of lukewarm water. Immediately after the bath the patient should have rest; he is therefore to be wrapped up in a dry sheet and put to bed (which may with advantage be warmed, especially at the foot), lightly covered, and given a glass of wine. In dealing with very feeble patients, one may begin with baths of a higher

* *Ziemssen*, Cyclopædia of the Practice of Medicine. Amer. edition, vol. I, p. 208.

temperature, say 75°, although of course these will produce less effect. A method, especially recommended in such cases, if the surroundings permit, is that recommended by Ziemssen, of baths gradually cooled down, beginning with about 95°, and adding cold water gradually until the temperature is reduced to 72°, or below. These baths should be of longer duration."

"As a rule, in somewhat severe cases, I have the temperature taken every two hours day and night. Whenever the temperature in the rectum reaches 103°, or in the axilla 102.2°, a cold bath is given. As a matter of course, however, individual peculiarities must be taken into consideration. In children, or in persons whom one has reason to suppose capable of great resistance to the influence of heat, the temperature which calls for the bath may be placed higher, say 104° in the rectum, or 103° in the axilla. In those, on the contrary, with less than the average resisting power, it may be well to employ the bath before so high a temperature has been reached, and according to the circumstances of the case, give a shorter bath, or a warmer one, or the gradually reduced bath of Ziemssen."

In following the above directions for the application of the cold bath in febrile diseases, however, it should be remembered that they were written in a cold, rigorous climate, like that of Germany; some allowance should therefore be made, on the other hand, for the semi-tropical one under which we live, where most of the people are accustomed to a certain amount of continuous heat of the weather almost throughout all seasons of the year.

It is hardly necessary to pass any remarks on the method of reducing the temperature of the body by permanently placing the patient upon a cot for the purpose of keeping up a continuous spray of cold water over the whole body,—the impracticability of which the inventor proved by paying with his own life for the unphilosophical idea of preventing the perspiration of the skin, and inducing a depression of the nervous system.

As regards the delirium I have to add that, in the epidemic of 1867, I have, in severe cases, frequently made use of a fly-blister to the nape of the neck, leaving it long enough to produce suppuration. The object, as may be guessed, was to invite the blood from the congested brain to the sore. But, although this practice

was generally followed by favorable results, I would not pretend to assert that they were solely due to the application of the blister, but rather suspect that the cold applications to the head, used at the same time, contributed their full share. In the succeeding epidemics I omitted the blister, and directed my attention chiefly to the proper application of the cold to the head, of which the results were equally favorable, and without giving so much trouble to the patient, as is always associated with the application of a blister in that locality.

The pain over the bladder, associated with a temporary retention of urine, frequently observed during the febrile stage, is generally relieved by the application of a warm flax-seed poultice with some laudanum poured over it, to be continued until the pain is relieved and the urine commences to flow.

The nausea and constant inclination to vomit during the febrile stage of the disease is very distressing to the patient, and difficult to allay. The application of a sinapism over the epigastrium affords sometimes relief, but not permanently. I have before remarked that the condition of the stomach is a sure index of the condition of the liver, and the latter of the condition of the whole organism; it is therefore important that the stomach should be examined from time to time, in order to ascertain whether it is sensitive to pressure upon it, or not. As long as there is no pain produced by the pressure there is no immediate danger to the patient, while, on the other hand, the production of pain by pressure indicates a highly congested condition of this organ and a considerable fatty infiltration of the liver, which possibly may be accompanied by a rupture of the minute vessels of the mucous membrane of the stomach, giving rise to black vomit. As soon, therefore, as the least tenderness is noticed, such measures as will induce a revulsion from that organ to the skin should at once be taken. In many cases a mustard cataplasm answers all purposes; in others, however, the emplast. cantharides must be resorted to.

In order to allay the thirst of the patient, small fragments of ice may be given to be dissolved in the mouth, or even to be swallowed entire; the moderate cold thus produced upon the mucous membrane of the stomach may contribute to restore to a cer-

tain degree the tonus of the minute blood vessels. The ice, however, must be given with discrimination, as an excessive cooling down of the stomach might at the same time exert a depressing influence upon the sympathetic ganglia of the solar plexus, situated in the close vicinity of this organ. The same danger will accompany the application of solid ice to the epigastrium for the purpose of arresting the black vomit. If the latter really occur, the most reliable remedy, perhaps, is the swallowing of small pieces of ice. Iced champagne is a favorite remedy with many physicians, and I have often ordered it myself, though I would not assert that it exerted a special influence upon the blood vessels of the stomach; if followed by good results it may be presumed that they were chiefly due to the ice.

If the patient has safely passed the febrile stage, accompanied by the hyperæmia of the brain, the chief danger during the second stage, especially if the delirium was severe, lies in the great depression of the nervous system, being mostly felt by the heart, but also by other organs, as the liver and kidneys. The depression of the heart's action, however, may be increased by the degeneration of a part of its muscular elements, occurring in severe cases, and which may lead to a paresis or even paralysis of this organ. For this reason, as soon as the febrile storm has passed, the action of the heart should be closely watched, and if found too weak for the performance of its function, stimulants should at once be administered. While some physicians make use of digitalis, carbonate of ammonia, etc., which may well answer the purpose, others, perhaps the greater number, prefer the alcoholic stimulants; for my own part, I have always used the latter, as they are generally ready at hand and answer the purpose equally as well. They must, however, be administered with great caution and discrimination, as by an excessive use they may do as much harm as good, by overstimulation being followed by a worse depression, or by irritating the stomach leading to black vomit. Unfortunately, they are but too frequently misapplied to the disadvantage of the patient; from all I know, brandy and whisky flow too freely during an epidemic of yellow fever, so much so, that the people have become accustomed to regard these liquids as the chief remedy for the disease. I have learned of cases in which they

have actually been given during the febrile stage of the disease, when they obviously can only increase the already existing excitement and augment the disturbance of the functions of the organs. On the other hand, however, I have met with cases, in which a tablespoonful of pure whisky, slightly diluted with water, and administered at the proper time, has evidently saved the patient's life by arousing the very much depressed action of the heart. As regards the selection of the stimulants, it may be said that while the ordinary wines, besides containing too little alcohol, are unsuitable on account of their excessive acidity and impurity, the finer sorts, like genuine old Sherry and Madeira, are too expensive and, also, difficult to be obtained. Pure brandy or whisky, therefore, will be the most preferable stimulants.

If during the course of the disease the urinary discharges are interrupted, the catheter, of course, should be used, in order to ascertain whether there is any urine in the bladder, or whether the non-appearance of this fluid is really due to a deficiency of secretion, depending upon the degeneration of the epithelium of the uriniferous tubules or the obstructions caused by the various infarctions in the latter. In those cases in which a suppression of the urinary secretion really occurs, it appears to me that nothing direct or reliable could be done to induce the kidneys to resume their functions, as the interruption depends upon the organic changes in these organs; though, if depending merely upon the infarctions of the tubules, especially the straight, these obstructions may be overcome, in some cases, and cleared by the pressure of the urine from behind them; the urine, then, will re-appear. On the whole, the stimulation of the nervous system appears to me here the proper course to be pursued; though, in such cases, the condition of the organs in general is already so low as to leave but very small chances for the recovery of the patient.

As regards the diet in yellow fever it may be said that during the febrile stage of the disease it is of little importance, for the reason that the patient generally refuses anything in the shape of food offered to him. Nevertheless, it appears to me that the stomach should not be left entirely empty during the stage, and some light nourishment in liquid form should be given. A thin soup of barley, or any other farinaceous liquid answers perhaps the

purpose best; and, if given cold, may at the same time serve to allay the thirst. In the second stage, small doses of the essence of beef—always freshly prepared—or milk will answer the purpose. It is sufficiently known that some caution should be observed during the convalescence in not over-feeding the patient, an error which may be followed by very serious consequences. The diet, therefore. should be chiefly albuminous, very digestible, and given in small doses at first, until the congestion of the stomach may have entirely disappeared. But, it is not only the stomach where the danger of over-feeding lies; for, though the food may be properly digested and the nutritive matters absorbed into the blood, the degenerated and weakened organs and tissues may not be able to assimilate them, and a new disturbance in their nutrition is apt to arise. Alcoholic stimulants also should be given in convalescence with considerable moderation; in most cases they are not needed at all, the proper nourishing food alone will be sufficient to restore the strength of the patient.

The above remarks may be regarded as mere outlines of a rational treatment of yellow fever, to be filled with the details by the good judgment of the practicing physician. A number of special medicines have been, besides, used in this disease by many physicians; but as they have not only failed to exert any influence upon the neutralization or elimination of the infectious poison, but perhaps rather done harm, I forbear to mention and discuss them. Nevertheless, I would by no means discourage the trial of certain remedies in this disease—empirical as the experiment may be—if administered upon some rational principle. For, if a specific remedy neutralizing the poison should ever be discovered, it will probably be by empirical experiment. Such experiments can only be advantageously made in a hospital, and by experienced physicians, accustomed to systematic scientific investigations; therefore, the general practitioner will do better by following the simple rules of treatment given above until some special and better method has been ascertained.

REMARKS ON THE PREVENTION OF YELLOW FEVER.

ALTHOUGH the subject of the prevention of yellow fever has always received the attention of the medical profession, it has never agitated the public mind to such an extent as since the occurrence of the epidemic of 1878. Aside from the numerous articles which have been written on this subject, so much has been said in speeches and lectures delivered, that I cannot properly conclude this treatise without likewise offering some brief remarks on the prevention of this disease.

Though, from all that of late has been said and written on this subject, it might be presumed that the prevention of a contagious disease was a most difficult and complicated task, it will appear more simple when examined closer, and in a systematic manner and form. Neither is there any novelty in the attempt made for the purpose of preventing disease, for this subject has been studied for many years by the scientific men of all civilized nations, most particularly during the last fifteen years, since the occurrence of the cholera epidemic in Europe; and the treatises and articles containing the results of the experiments and investigations relating to it are quite numerous, forming a considerable part of the medical literature of these years. Besides, many of these experiments have been made in so thorough a manner, that, without addition, they may equally serve as a safe basis in devising means for the prevention of yellow fever.

As a contagious disease can only be prevented by the destruction of its specific cause, it is obvious that the *true nature* of the latter must *first be ascertained*, before any reliable means could be devised to arrest its activity. Without this knowledge the means employed will be *empirical* in their application, and in most instances, *as experience has sufficiently shown*, be attended with *a failure* of the object in view. Thus, if the disease, as some suppose, is generated by the gases arising from decomposing

animal and vegetable matter, the destructive agent, or so-called "disinfectant," should possess the property of neutralizing these gases; or, if, according to another theory, it is produced by the presence of minute organisms contained in the air we breathe, the disinfectant should be destructive to the lives of these beings, and, accordingly, be brought into close contact with them; or, again, if depending merely upon certain climatic or meteorological conditions, as some people suppose, there can be no hope for relief, unless the climate could be changed; and, lastly, if propagated by morbid secretions derived from the diseased organism itself, the disinfectant should be capable of decomposing the poison.

Supposing the theory which teaches the origin of yellow fever from gases arising from decomposing animal and vegetable matter in the streets and houses of a city to be true, then the means of prevention would be quite simple, consisting in keeping the streets and the interior of houses clean from this matter, with fair prospects of being delivered from the yellow pestilence. But though clean streets and houses are very recommendable, and indicate a certain degree of civilization, this theory, as far as it concerns yellow fever, rests, for the reasons already given, upon a very weak foundation.

Closely allied to this theory is the "bilge-water" theory, according to which the cause of the disease is to be sought either in the gases arising from this liquid, or in the minute organisms which it contains. If this theory was as true as it is false, there would be no difficulty of keeping yellow fever from our shores, as there is no want of agents which would neutralize the gases, or kill the organism, in a circumscribed space like the hold of a ship, though the proposed freezing process, having no rational foundation, would, like other empirical experiments, prove a decided failure.

Greater difficulties, however, would be encountered in the prevention of yellow fever, if the disease depended upon the presence of minute organisms contained in the air and breathed by the people, as here, the only effectual mode of destroying the cause would consist in bringing the organisms into actual contact with some disinfectant agent, as, for instance, carbolic acid *in solution*. Accordingly, every little corner of the streets and

houses, as well as the furniture, bedding and clothes of the people should be wetted with this solution, a task impossible to be accomplished. To use the disinfectant in a gaseous form would be equally as impracticable, for the reason that, in order to destroy the organisms, it would be necessary to use the gas in such a concentrated form as to cause the death of the surrounding people, before it would in the least affect the organisms. For ten successive years the streets of New Orleans have been sprinkled over with carbolic acid solution, without ever having made the slightest impression upon the cause of yellow fever. It must, therefore, have now become obvious that unless these or similar measures are carried out in a most thorough manner, it is useless to resort to them at all.

If yellow fever were really caused by noxious gases arising from animal and vegetable decomposition in the streets and houses, or by the bilge-water in the ships, or by bacteria or other minute organisms, the prospects of mitigating or preventing the disease would not be very encouraging, as dirt and filth will occur in any large city, and in defiance of the best regulated and executed sanitary laws. But, fortunately, this is not the case, as it is more probable that its true cause is a specific animal poison, similar in nature to that of small-pox, scarlet fever, or other contagious diseases, or to other animal and vegetable poisons,—substances, the noxious influence of which may, with the proper caution and attention, be counteracted, or, at least, to a certain degree limited.

In the preceding pages I have already sufficiently demonstrated the nature of the poison, and the manner in which it is propagated and carried from place to place, but have omitted to offer any remarks on the proper mode of prevention. In entering upon this subject it becomes necessary, first, to inquire in what manner the poison is probably introduced, or called into activity in a community. Thus, if yellow fever should appear at New Orleans, or any other seaport, *after having been entirely absent for several years*, it is very probable, or *almost certain*, that its poison has been imported anew, and most likely by ships hailing from infected ports. But, if the disease should re-appear in a place one or two years, or even longer, after having prevailed there, the prob-

ability arises that the poison is derived from the previous cases, having remained in the interval of time in a dormant (condensed) state, *i. e.*, for the want of the conditions necessary to its re-assuming the vaporous or gaseous form, as already explained. This probability, however, does not preclude a simultaneous fresh importation. While thus the poison may, on the one hand, be newly imported by ships, it may also lurk about from year to year in the same place, as is the case with small-pox, scarlet fever, measles, etc., the communicability of which nobody doubts. The extent to which the disease may spread, after having originated in this manner, cannot be determined, as it depends on various circumstances or so-called "chances." It is more than probable that those sporadic cases, occurring almost every year, and whose origin cannot be traced, arise from these sources; and it is certain that the yellow fever epidemic of 1879, in Memphis, originated from the poison which, by adhering to the old clothes, had over-wintered in the shoemaker's box. It will be remembered that in this epidemic the first cases occurred in one and the same neighborhood, and were confined to certain houses or families.

From the numerous experiments made relating to the nature of animal poisons or contagia and their disinfectants, almost every investigator has drawn the conclusion that the contagion will lose its noxious properties by a free exposure to the atmosphere, and that for this reason the latter, promoting the process of oxidation, is the best disinfectant; while, on the other hand, the poison will retain its properties when kept in a place from which the atmosphere and light are excluded. Now, it is well known that after an epidemic of yellow fever, the majority of people in whose houses cases and deaths have occurred, *do not destroy or even properly disinfect* the bedding or other articles to which the poison emanating from the patients has adhered; but that, on the contrary, especially among the lower walks of life, these articles are left as they were, and, in many instances, kept in dark and badly ventilated places, where there is no opportunity for the destruction of the poison by oxidation. As soon as the heat of the summer returns, and is accompanied by a certain degree of moisture, that portion of the poison, as yet not destroyed

by oxidation or dry heat, will commence to be vaporized, and, if breathed by any individual susceptible to the disease, will manifest its activity in the production of the phenomena characterizing yellow fever. The first case thus produced may recover without its true nature ever being suspected, while the disease may nevertheless be communicated to other persons, and thus have existed for some time until a severe case, characterized by unmistakable and prominent symptoms, such as black vomit, occur. Under such circumstances the tracing back of the disease to the first case generally proves a failure.

These facts will show that in the prevention of yellow fever our attention must be directed toward two chief objects, viz., the prevention of its fresh importation, and of its spreading after once having made its appearance, and, furthermore, the sure destruction of the poison generated by the cases arising.

The first object, of course, can only be attained by a properly arranged and conscientiously executed *quarantine*. So much has been said and written of late, both officially and publicly, about this subject—especially by those who claim its study as a specialty—as to require no additional remarks. Nevertheless, it may be said that the subject of quarantine has been presented as being much more complicated than it really is. Quarantine is quite an old institution, and has been practiced by many nations for many years. And it is more than certain that properly regulated and executed systems of quarantine do exist to-day, and, from all I have learned, even in our own country, which, moreover, might well serve as pattern for those stations along the coast of the Mexican Gulf, established for the purpose of preventing the importation of yellow fever. But though the administrative part of a quarantine may be quite simple, *as long as performed by intelligent and faithful officers*, the selection and application of a suitable disinfecting agent is more difficult; for, if this fail to destroy the yellow fever poison, when really present, the whole system of quarantine must appear a needless farce. The experiments made for the purpose of ascertaining the efficiency of a proper disinfectant must be made on matter, similar in nature to that representing the poison of contagious disease, and, as I have once hinted before in a short paper "On the Pathology of Yellow Fever"—

published in the *New York Medical Journal*, Febr., 1879,—the fresh or dried lymph of the cow-pock-vesicle seems to be the most suitable for this investigation. A number of experiments of this kind have already been made by *Dougall*, *Baxter*, *Braidwood* and *Vacher*, all accompanied by nearly the same results. The summary of the results which Baxter obtained,—who extended his experiments even to the virus of infectious inflammation of guinea-pigs, and to glanders— is stated in his report as follows: *

1. "Evidence has been adduced to show that carbolic acid, sulphur dioxide, potassic permanganate, and chlorine, are all of them endowed with true disinfecting properties, though in very various degrees."

2. "It is essential to bear in mind that antiseptic is not synonymous with disinfective power, though, as regards the four agents enumerated above, the one is, in a certain limited sense, commensurate with the other."

3. "The effectual disinfectant operation of chlorine and potassic permanganate appears to depend far more on the nature of the medium through which the particles of infective matter are distributed, than on the specific character of the particles themselves."

4. "When either of these agents is used to disinfect a virulent liquid containing much organic matter, or any compounds capable of uniting with chlorine, or of decomposing the permanganate, there is no security for the effectual fulfilment of disinfection short of the presence of free chlorine or undecomposed permanganate in the liquid after all chemical action has had time to subside."

5. "A virulent liquid cannot be regarded as certainly and completely disinfected by sulphur dioxide unless it has been rendered permanently and strongly acid. The greater solubility of this agent renders it preferable, *cæteris paribus*, to chlorine and carbolic acid, for the disinfection of liquid media."

6. "No virulent liquid can be considered disinfected by carbolic acid unless it contain at least two per cent. by weight of the pure acid."

**Reports* of the *Medical Officer of the Privy Council and Local Government Board*.— London. 1875.

7. "When disinfectants are mixed with a liquid, it is important to be sure that they are thoroughly incorporated with it; that no solid matters capable of shielding contagium from immediate contact with its destroyer be overlooked."

8. "Aërial disinfection, as commonly practiced in the sick-room, is either useless or positively objectionable, owing to the false sense of security it is calculated to produce. To make the air of a room smell strongly of carbolic acid by scattering carbolic powder about the floor, or of chlorine, by placing a tray of chloride of lime in a corner, is, so far as the destruction of specific contagia is concerned, an utterly futile proceeding."

9. "When aërial disinfection is resorted to, the probability that the virulent particles are shielded by an envelope of dried albuminous matter, should always be held before the mind. Chlorine and sulphur dioxide are, both of them, suitable agents for the purpose; the latter seems decidedly to be the more effectual of the two. The use of carbolic vapor should be abandoned, owing to the relative feebleness and uncertainty of its action Whether chlorine or sulphur dioxide be chosen, it is desirable that the space to be disinfected should be kept saturated with the gas for a certain time, not less than an hour; and this in the absence of such gaseous compounds as might combine with or decompose the disinfectant, and so far impair its energy."

10. "When the thorough disinfection of a mass of solid or liquid matter, through which a contagium is disseminated, is impracticable, we should guard against giving a false security by the inadequate employment of artificial means. It is probable that all contagia disappear sooner or later under the influence of air and moisture, and that the absence of these influences may act as a preservative. When, therefore, we cannot advantageously or effectually supersede the natural process of decay, we must be sure that we do not hamper it by the injudicious use of antiseptics."

11. "Dry heat, when it can be applied, is probably the most efficient of all disinfectants. But, in the first place, we must be sure that the desired temperature is actually reached by every particle of matter included in the heated space; secondly, length of exposure and degree of heat should be regarded as mutually compensatory factors, within certain limits."

The above rules, laid down by Baxter for liquid or aërial disinfection, are very simple and will suffice for all purposes. In applying them, however, to the disinfection of ships, it will be found that a perfect disinfection of the whole cargo of a ship is almost impossible as long as the latter remains undisturbed, for the reason that the gaseous disinfectant cannot penetrate to its depth, or into the interior of the bales of merchandise, unless the ballast is broken. In order to thoroughly disinfect the latter, therefore, it must be broken, by unloading the ship and exposing it to the free atmosphere. Now, whether such a proceeding would be practicable, I am unable to decide, not being sufficiently acquainted with the commercial details and difficulties attending such an undertaking. I can only point to the fact, that unless every part of the cargo is exposed to the influence of the disinfectant or the atmosphere, any other mode of disinfection will be useless.

But, even, if the breaking of the ballast were practicable, a proper inquiry should first be made whether such a complicated labor is really necessary, that is, whether the noxious poison of yellow fever were, indeed, adhering to the merchandise of the cargo. Although I would not venture to deny the possibility of the poison being carried by the cargo of a ship hailing from the sea-ports of the West Indian Islands, or of the coast of South America, and consisting, as far as I know, generally of coffee, sugar, tobacco, etc.—articles which are generally kept in large warehouses—I cannot but think that such an occurrence must be very rare, unless these warehouses are situated in a densely populated locality where the yellow fever is raging, and the goods are handled by persons who have come into direct contact with yellow fever patients. And even, if this were the case, it appears that during or before the act of loading, the goods, generally lying along the wharves of the port, become sufficiently exposed to the atmosphere to render the vaporization and ultimate diffusion of the poison into the latter possible. It is, therefore, more probable that the poison is generally carried to a ship by the clothes of the sailors and passengers, as well as by the effects locked up in their trunks; and it is from these that the poison is communicated to the usually badly ventilated and confined spaces and cabins of the ship during the voyage. This supposition will appear more rea-

sonable in considering the nature of those places and localities in a sea-port, generally visited by the sailors when on land.

If the view I have taken is correct, a thorough disinfection of the clothes and effects of the sailors and passengers, together with the cabins and general hold of the ship, would be all that is needed.

The disinfection of the ship may be effected in accordance with the general rules laid down by Baxter, together with the washing of the deck and other wood-work. But as regards the clothes and effects of the passengers, the application of dry heat is preferable, as it is more reliable in its effects. This method of disinfection has been practiced for a number of years in European hospitals, both in England and Germany, and different apparatuses have been constructed for the purpose, the description of which may be found in the medical records. With the construction of the proper buildings and accommodations of a quarantine station, arrangements could be made that, while the clothes and other effects of the passengers are exposed to the dry heat of the disinfecting apparatus, they, themselves, might enjoy a good bath, for soap and water will prove, after all, the best disinfectant.

The degree of heat which woolen or other goods are able to bear without damage in the heated chamber during the process of disinfection has been determined by *Vallin.** He found that white blankets, if exposed to a temperature of 110° C. for two hours, slightly change in color, such as if they had been washed with hot water; if exposed to 115-120° for two hours, a slight yellowish coloration was noticed. Linen or cotton goods bear 115° very well, their color suffering only when exposed to 125° for two hours. The integrity of the goods becomes affected with a much higher (150°) temperature. Change in color occurs sooner with dry heat then when the heated air contains a large quantity of moisture. As regards the degree of heat required to destroy infectious matter, it appears that most germs of disease become innoxious with a temperature of 100° C., the septic matters, however, retain their power of infection even at this temperature.

The prevention of the yellow fever, after having been once introduced, or newly arisen—*events, possible in the face of the best*

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* *Virchow u. Hirsh*, Jahresbericht f. d. Jahr 1877. vol. I. p. 507.

sanitary regulations,—appears to me no less important, and much more difficult, than to guard against its importation. Though it may be nearly impossible to extinguish the disease abruptly after it has once arisen, much can be done to prevent its spreading to a much greater extent, or from finally assuming the form of an epidemic. The only way by which this can be acccomplished is to prevent, or, at least, restrain the intercourse between the healthy and the sick. I have already pointed to the most pernicious custom of the female neighbors entering indiscriminately the house in which a patient lies sick of yellow fever, either to inquire after his welfare, or for idle curiosity. Now, though the first of these objects is very laudable, it must be dispensed with, when associated with the danger of carrying the poison to other houses and families, from which it may eventually spread over the same or other districts. Any one, who will reflect upon the complexity of the daily intercourse between the inhabitants of a large city, will become convinced of this fact. The first step, necessary to the prevention of the spreading of the disease, must therefore consist *in informing the people of the contagious nature of the disease, and showing them the danger of entering a house infected with the disease. There remains no doubt that extensive epidemics have chiefly been due to the idea of the non-contagiousness of yellow fever, prevailing among the people.* In advocating the strictest observance of non-intercourse with cases of yellow fever, I, of course, exclude those persons necessary to attend to the comfort and nursing of the patient. It is not my part to point out in this place the details of the manner in which this proposition may be carried out without too much inconvenience to the friends of the patient, but I am confident that with the proper system and precaution it can be done, and the disease be arrested, or kept in safe check until the colder weather sets in, when the fall of the temperature of the air will prevent the evaporation and diffusion of the poison.

Equally as important as the isolation of the cases is the complete disinfection or destruction of all objects to which the exhalations of the patient may have adhered during the course of the disease. Those articles with which the patient has come in immediate contact, such as bedding, shirts and other garments,

should absolutely be burned, as soon as the patient is in convalescence, even if it should be done at the cost of the community, for it would be the cheapest mode of proceeding in the end. Such articles as will stand boiling and washing with soap should undergo the process, for, it may safely be guaranteed that the noxious poison, arriving in the gutters of the street after this procedure, will be surely deprived of its noxious properties; woolen articles may be disinfected by heat. As the poison adhering to the floors, doors and windows of the house is most effectually removed by plenty of soap and water, nothing would remain but the walls, which, if admissible, might be white-washed, or, if papered, thoroughly disinfected by one of the disinfectants in gaseous form, as recommended by Baxter.

From the above sketch it may be inferred that the prevention, or, at least, the checking of yellow fever, is not as difficult a task as might be supposed, if the proper precaution is observed, and the necessary means are conscientiously and systematically employed. A most important factor in the execution of these measures, however, will ever be the active co-operation of the inhabitants of the city themselves; the submission to some inconvenience by the individual for the welfare of the whole community, even at the sacrifice of a few individual rights.

EXPLANATION OF THE ILLUSTRATIONS.

The accompanying drawings were made from microscopical sections stained with carmine; therefore, the higher or lesser degree of their shading indicates the higher or lesser degree of the staining of the different anatomical elements. In the same manner is the pigmental infiltration of hæmoglobin (Figs. 3 and 5) indicated by a darker shading. The existing relation between the degree of degeneration of the parenchymatous cells and that of staining will be found explained in the text.

Fig. 1.—Section of yellow fever liver—general type ; *a*, radicle of a hepatic vein (intra-lobular). The section of the vessel on the right side belongs to a portal (inter-lobular) vein. The capillaries are empty, the hepatic cells filling up the meshes of the latter, are seen infiltrated with fat globules. (Magnified 50 diam.)

Fig. 2.—Section taken from the same liver, and more highly magnified, showing the very termination of a portal (inter-lobular) vein ; *a*, remains of the adventitia of the venule ; *b*, capillaries ; *c*, fat-globules. Those capillaries in the immediate vicinity of the vein still contain blood-corpuscles. (Magnified 275 diam.)

Fig. 3.—Section of yellow fever liver, with infiltrations of hæmoglobin ; *a*, longitudinal section of an intra-lobular vein. The hepatic cells in the vicinity of its termination are seen infiltrated with hæmoglobin ; *b*, transverse section of a portal vein, with some of its radicles—no infiltration of hæmoglobin is seen around it ; *c*, transverse section of an intra-lobular vein, surrounded by an infiltrated portion of parenchyma. (Magnified 50 diam.)

Fig. 4.—Section of a cirrhosed liver, showing the fatty infiltration of the cells, caused by yellow fever in the interior of the lobules. The hepatic cells of the periphery of the lobules present a blackish-green color, due to the presence of bile-pigment. (Magnified 50 diam.)

Fig. 5.—Section of a yellow fever stomach, showing the congestion of the veins, the infiltration of hæmoglobin, and the extravasation of blood caused by a rupture of the minute veins or larger capillaries ; *a*, glandular layer, and *b*, muscular layer of the mucous membrane : *c*, submucous connective tissue. The congested vessels descending through the glandular layer represent those straight venules formed by the venous radicles arising from the network of large capillaries beneath the epithelium, and surrounding the orifices of the gastric glands. The dots, seen throughout the muscular layer, represent transverse sections of muscular fiber-cells. (Magnified 50 diam.)

Fig. 6.—*a*, congested venous radicles, as seen upon the mucous surface of the stomach, and *b*, congested portion of the network of large capillaries, forming the red patches observed upon the mucous membrane of this organ, as described in the text. (Magnified about 5 diam.)

Fig. 7—Vertical section of a yellow fever kidney from near the surface; *a*, albuminoid cylinders, deeply stained with carmine; *b*, side view of the epithelium of the uriniferous tubules; *c*, basement-membrane. Toward the right side of the drawing (near the letters *b* and *c*) the almost transverse sections of two cylinders are seen, with granules imbedded into the albuminoid substance. (Magnified 275 diam.)

Fig. 8.—Five uriniferous tubules, containing different kinds of infarctions, as described in the text; *a*, albuminoid cylinder, with epithelial cells and the remaining fragments of broken-down cells embedded in the albuminoid substance; *b*, epithelium; *c*, basement-membrane; *d*, empty portion of the tubule, with cellular remains; *e*, remains of nuclei and cells. (Magnified 275 diam.)

Fig. 9.—Section of two uriniferous tubules, cut more or less transversely, and containing infarctions formed by the remains of degenerated cells; some of the latter are deeply stained with carmine, representing the first stage of degeneration, as described in the text. (Magnified 275 diam.)

Fig. 10.—Transverse section of a number of uriniferous tubules. While the epithelium of the greater number of these tubules has a normal appearance, the cells of four tubules (*a* and *b*) are deeply stained with carmine and of a glistening appearance, representing the first stage of degeneration; *b*, one of the latter tubules, the lumen of which is filled up by a cylinder. (Magnified 275 diam.)

Fig. 11.—Nearly transverse section of a uriniferous tubule, with degenerated epithelium, a portion of which has undergone fatty degeneration. (Magnified 275 diam.)

Fig. 12.—A number of uriniferous tubules, lined by an apparent normal epithelium, though the lumen of three tubules is filled up by minute masses of fat. (Magnified 275 diam.)

Fig. 13.—Collecting tubules of the medullary substance, showing the beginning of fatty degeneration; *a*, degenerated epithelial cells, with fat-globules; *b*, side view of the remaining epithelium; *c*, basement-membrane; *d*, inter-lobular vessels filled with blood-corpuscles. (Magnified 275 diam.)

Fig. 14.—A uriniferous tubule from the medullary substance, containing degenerated epithelium and fat; the fat-globules have become fused with each other, and are drawn out, by the passing urine, in long, thread-like masses; *a*, degenerated epithelium; *c*, side view of the same; *c*, basement membrane; *d*, fatty thread-like masses. (Magnified 275 diam.)

Fig. 15.—Portion of a tubule of the medullary substance, with degenerated epithelium, and filled with fat-globules; *a*, degenerated epithelium; *b*, side view of the same; *c*, basement-membrane. (Magnified 275 diam.)

Fig. 16.—A small portion of the semi-lunar ganglion, showing four ganglionic bodies, the nuclei of which have disappeared; in one of them (on the left side) the nucleus is still observed. (Magnified 275 diam.)

Fig. 17.—Connective tissue cells of the pia mater, observed (only in one case) to multiply by division. (Magnified 275 diam.)

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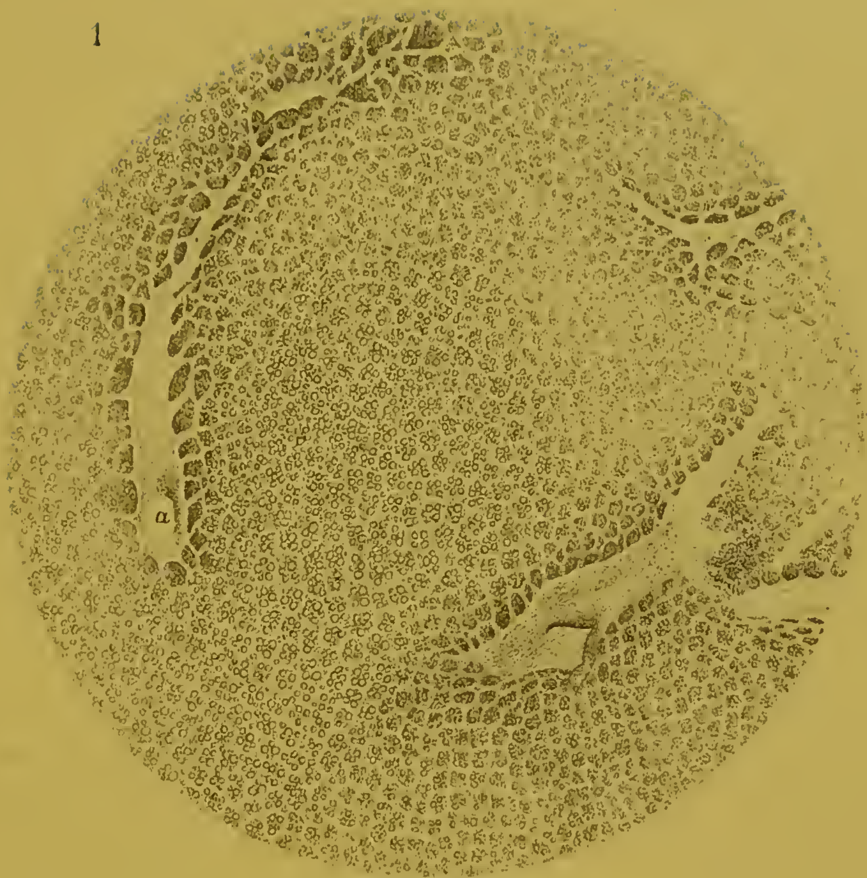

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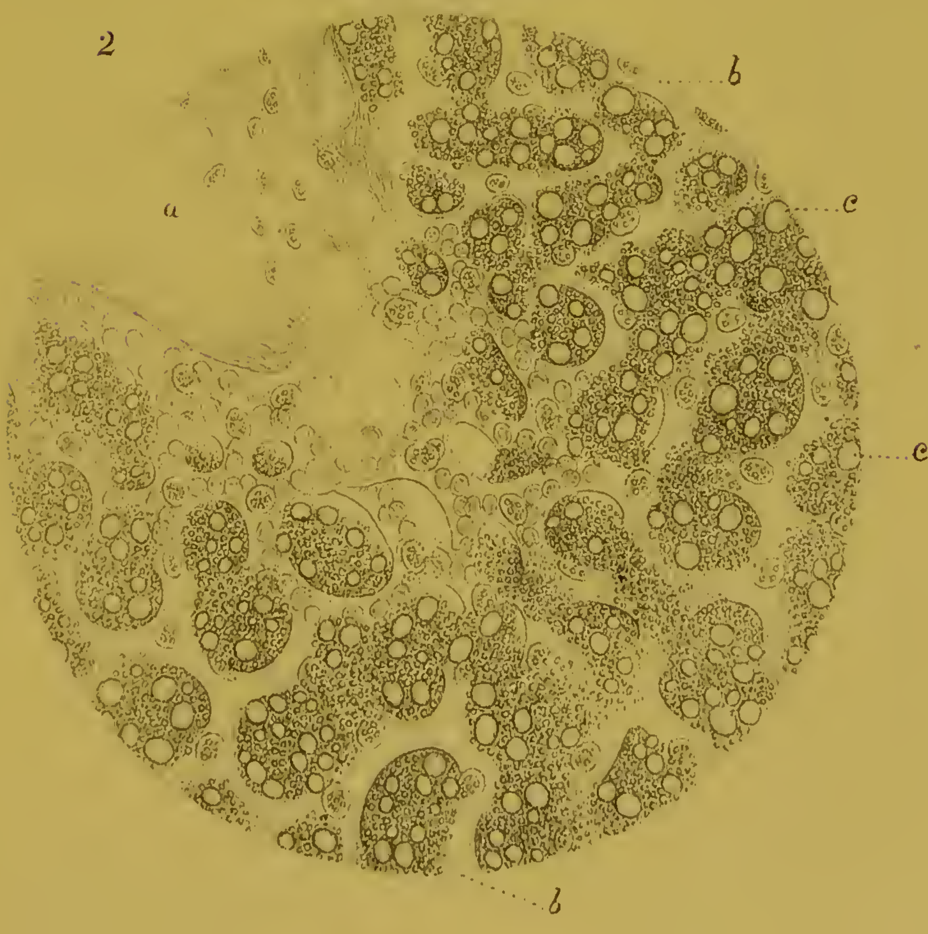

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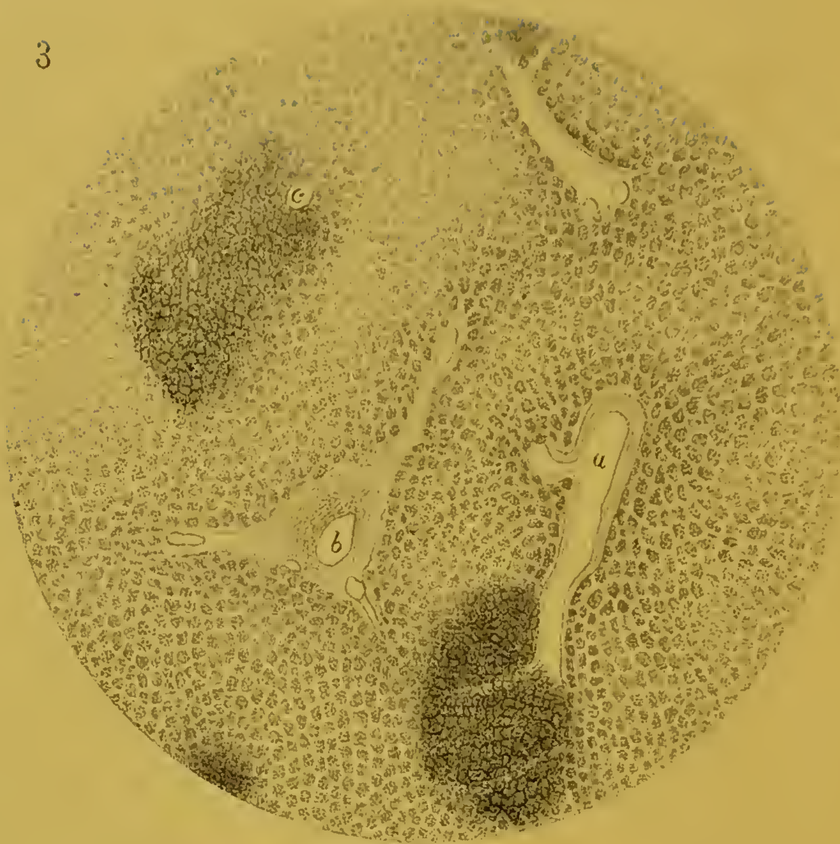

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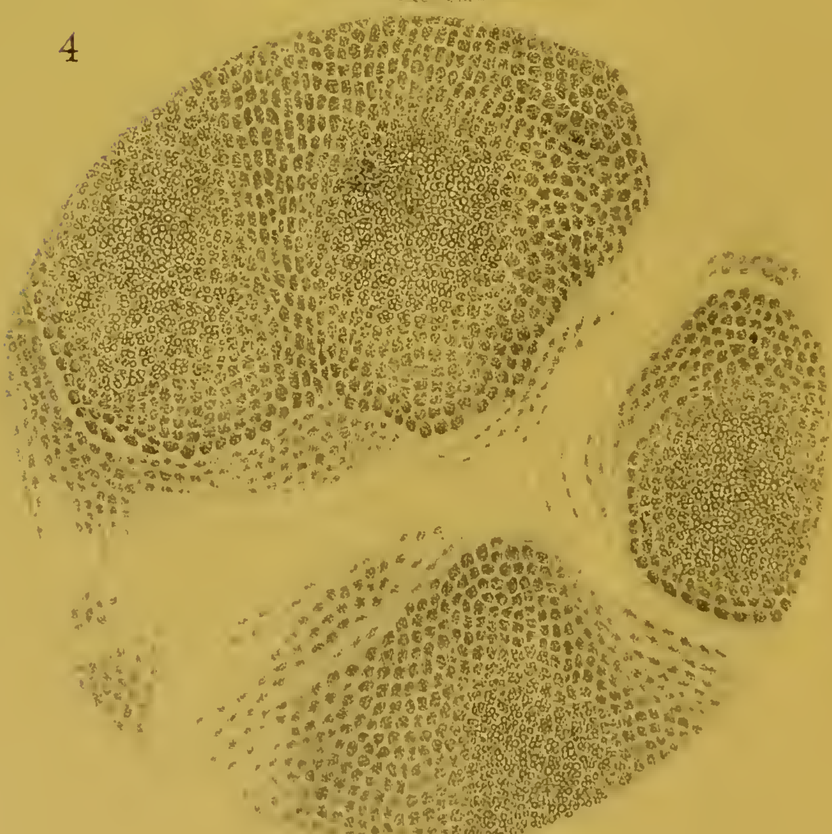

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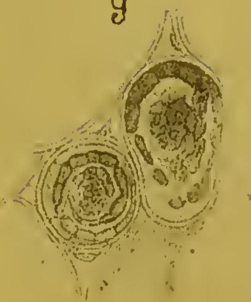

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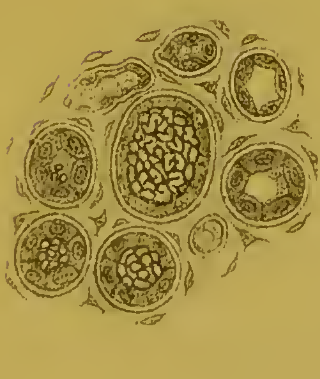

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